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Pathology

801. **An "Auto-immune" Reaction against Human Tissue Antigens in Certain Chronic Diseases**
D. C. GAJDUSEK. *Nature* [*Nature* (*Lond.*)] **179**, 666–668, March 30, 1957. 2 refs.

This paper from the Walter and Eliza Hall Institute of Medical Research, Melbourne, reports the demonstration of specific complement fixation, sometimes in very high titre, in the serum of patients suffering from various diseases by antigens which were prepared from human liver, kidney, and muscle, and rat liver and kidney tissue.

The antigens were prepared from the tissues as soon as possible post mortem, a 10% suspension of finely ground tissue in saline being clarified by 3 centrifugations at moderate speed and the crude supernatant fluid being used as antigen. The effective antigenic agent was subsequently associated with the material sedimenting on centrifugation at 35,000 *g* for 45 minutes.

Complement-fixation was found rarely in sera from 21 normal subjects and from a series of 124 patients with miscellaneous diseases, including acute and chronic infective conditions and neoplasms, only one of the former and 2 of the latter giving high-titre positive reactions. Positive reactions were obtained in 9 out of 11 cases of disseminated lupus erythematosis, 3 out of 4 cases of "lupoid hepatitis", 11 out of 25 cases of other types of chronic hepatitis, and 2 out of 5 cases of macroglobulinaemia [clinical diagnosis unstated], the numbers giving high titres being 7, 1, 10, and *nil* respectively. A high titre of complement fixation to one human tissue antigen preparation was usually associated with similarly high titres to the other human and the rat tissue antigen preparations. All the activity of the sera was found to reside in the γ-globulin fraction. No correlation was obtainable with the results of tests for cold agglutinins and heterophile antibodies, the Wassermann, Kahn, and Weil–Felix reactions, the direct Coombs test for incomplete antibody, and various specific agglutination reactions.

The hypothesis of pathogenetic auto-antibody reactions has been put forward by many authors—especially in relation to the collagen-disease group—but the present author is careful to emphasize that whereas the observations reported could be interpreted as evidence of the production of such antibodies, it is also possible "that we are dealing with an adventitious reactivity of serum globulins not arising as a specific response to tissue antigen". *Harry Coke*

EXPERIMENTAL PATHOLOGY

802. **Toxic Effects of Mixtures of Sulphur Dioxide and Smoke with Air**
R. E. PATTLE and F. BURGESS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **73**, 411–419, 1957. 6 refs.

It has been suggested that sulphur dioxide is adsorbed by smoke particles in smogs and that this may enhance their lethal effect. The present authors tested this hypothesis by exposing guinea-pigs and mice to SO_2 alone and to SO_2 mixed with smoke. In the case of the mice the addition of smoke to SO_2 caused a 3- to 5-fold increase in the lethal effect of the exposure. This they attributed to a simple additive effect. One curious observation was that mice previously exposed to smoke survived exposure to SO_2 very much better than mice not previously exposed to smoke. The effect on mice of smoke which had previously been exposed to SO_2 was compared with the effect of smoke not so exposed. There were no fatalities from either, suggesting that there was no significant adsorption of SO_2 by the smoke. It is suggested that the protective effect of exposure to smoke on mice subsequently exposed to SO_2 was due to a reduction in the respiratory volume of the animals or to stimulation of the production of protective secretions. The authors point out that the concentrations of SO_2 used in their experiments were far in excess of those experienced in city smogs; nevertheless, they conclude that the results "provide strong negative evidence for the absence of any biologically significant interaction between SO_2 and smoke". *John Pemberton*

803. **Enzymatic Elucidation of the Relationship between Collagen and Elastin: an Electron-microscopic Study**
M. K. KEECH and R. REED. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 35–62, March, 1957. 38 figs., 8 refs.

In this study of the relationship between collagen and elastin, carried out at the University of Leeds, a preparation of dermal collagen from a 2-year-old child was subjected to the action of collagenase for 24 hours at 37° C. in phosphate buffer of *p*H 7·3; this resulted in 85 to 90% being dissolved. Under the electron microscope the residue showed an altered appearance which probably represented partial breakdown of collagen fibres and which has been named "moth-eaten fibres" (M.E.F.). These fibres, thus defined, formed the starting

point of the present study, in which they were subjected to the action of the following enzymes: elastase, hyaluronidase, and further collagenase, as well as to ultrasonic irradiation, with appropriate controls. The morphology of M.E.F. under these conditions was followed by systematic and quantitative observation under the electron microscope. All these agents produced a change in the fibres into structures ultramicroscopically resembling elastin.

In the second part of the study, powdered ligamentum nuchae elastin (prepared by the accepted method of boiling the ligament with 1% acetic acid for one hour), which ultramicroscopically appeared to be collagen-free, was subjected to collagenase. The enzyme dissolved the elastin, at first revealing collagen fibres which had presumably been previously covered and obscured by elastomucin and thus protected in the preparative procedure. Subsequently these collagen fibres were in turn dissolved. M.E.F. (or structures closely resembling them) were produced under these conditions, and showed changes on further collagenase digestion comparable with those shown by the M.E.F. from dermal collagen. These and other morphological changes observed are described and illustrated in detail, and are presented as further evidence of the ability of collagen to undergo change into elastin. M.E.F. appear to be intermediate structures in this change. *Allan St. J. Dixon*

804. **The Action of Cortisone and Anterior Corticotropic Hormone on Experimental Gastritis and Gastric Ulcers**

A. Rodriguez-Olleros and L. Galindo. *Gastroenterology* [*Gastroenterology*] **32**, 675–688, April, 1957. 7 figs., 46 refs.

The effect of ACTH and cortisone on the course of experimentally induced lesions of the stomach and duodenum was studied at the University of Puerto Rico. Gastritis and erosions were induced in 18 dogs by intramuscular injection of pancreatic juice (triple strength " panteric " powder buffered to a *p*H of 7·4 by potassium phosphate and disodium phosphate). Ten of the animals were also given daily injections of 30 to 40 mg. of cortisone starting on the third to the fifth day; the remaining 8 dogs served as controls. The erosions occurred mainly on the lesser curvature and pyloric antrum and duodenum and were usually punctiform in type. There was no difference between the control and cortisone-treated groups in the rate of healing of the gastric lesions.

In a further series of experiments in dogs " atrophan " (cincophen) was given in aqueous suspension by catheter in amounts of 2 g. daily for 4 days. With this procedure an ulcerative gastritis was produced. Cortisone in a dosage of 40 mg. daily was given in addition to cincophen to a group of 10 dogs who had been given the latter drug for up to 8 days. The addition of cortisone did not increase the erosive gastric lesions and did not hinder the healing tendency of cincophen-induced ulcers. The authors conclude that neither cortisone nor ACTH has any influence on experimentally induced gastric ulcers, but that " spontaneous " human ulcers may be affected by these hormones. *I. McLean Baird*

805. **A Virological Study of Certain Human Tumours.** (Опыт вирусологического изучения некоторых опухолей человека)

A. D. Timofeevskiĭ. *Архив Патологии* [*Arkh. Patol.*] **18**, 14–21, No. 8, 1956. 7 figs., 24 refs.

Extracts of various malignant tumours, including cancer of the stomach, breast, and lung, melanoma, sarcoma, and some malignant tumours of the central nervous system, were studied by means of electron microscopy. In about one-half of the specimens virus-like globular bodies were found, the size of which appeared to be between 40 and 100 millimicrons. The author claims that these bodies could be cultivated through several passages in tissue cultures on chorion-allantoic membrane of chick embryo " infected " with extracts of the malignant tumours. In some cases the " organisms " seemed to multiply during the passage. The author admits that although serological reactions seemed to confirm the specific character of these bodies, there is so far no direct evidence for their aetiological role in the development of malignant tumours. He adds that in control cultures of normal tissues similar bodies were found in a few instances. *F. S. Freisinger*

806. **Some Principles of Carcinogenesis Determined from the Results of Experimental Investigations.** (О некоторых закономерностях канцерогенеза (по данным экспериментальных исследований)

I. M. Neiman. *Архив Патологии* [*Arkh. Patol.*] **18**, 3–13, No. 8, 1956. Bibliography.

The experimental production of cancer usually requires prolonged treatment of the animal's skin with some carcinogenic agent. In some cases, however, a single treatment has proved to be sufficient, especially if it was followed by application of a non-specific agent such as croton oil. Berenblum called this phenomenon " co-carcinogenesis ". Application of the agent without the carcinogen proper has no carcinogenic effect in itself. Such a co-carcinogenic effect may be observed not only at the site of the original application of the specific substance, but in all parts of the body: thus Sinoi has shown that after treatment of the back with methylcholanthrene, the painting of the abdomen with croton oil produces tumours on both the back and abdomen.

It seems that small doses of carcinogenic substances, insufficient to produce tumours themselves, are able to " sensitize " the whole organism towards malignancy. Simpson has reported (*Cancer Res.*, 1947, **7**, 727) that after the application of methylcholanthrene dissolved in anhydrous lanoline on the back, where it is poorly absorbed and thus insufficient to cause a tumour, additional non-specific mechanical or thermal irritation at the site may produce cancer; or again it has been shown that an additional dose of methylcholanthrene injected subcutaneously at a distant site may cause cancerous growth at the site of the original application of the lanoline mixture and cause sarcoma to arise and grow around the oil depot more quickly than in control animals. This process of " sensitization " seems to require time to develop; thus cancer can be produced by quite small doses of methylcholanthrene (0·9 mg.)

when this is applied at long intervals (3 weeks), whereas when applied at short intervals (such as every second day) then a total dose of 42 mg. is needed to produce the same effect. In his own experiments the present author has shown that after the application of methylcholanthrene in sub-carcinogenic doses (5 treatments with a 0·5% solution in benzene) renewed application 5 to 8 weeks later produced cancer much more quickly and easily. Discussing the phenomenon of "sensitization by small doses" the author speculates whether this could result from small amounts of the carcinogenic substance still circulating in the blood or from some unknown nervous mechanism.

[This review is based to a great extent on previous reports in the literature and only a small part on the author's own experiments.] *F. S. Freisinger*

CHEMICAL PATHOLOGY

807. **Electrochromatography of Boron**
W. H. HILL, J. M. MERRILL, and B. J. PALM. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **15**, 152–159, Feb., 1957. 5 figs., 20 refs.

Boron has hitherto received little attention from the point of view of industrial hygiene, but the increasing use of boron compounds, particularly boranes and the organic esters of boric acid, has led the authors, working at the School of Public Health, University of Pittsburgh, to devise a method by which trace quantities of boron in biological and other materials can be detected semi-quantitatively by means of electrophoresis and a colour reaction with turmeric.

The method is as follows. Strips of Whatman paper No. 1 are each marked with a starting line 4 inches (10 cm.) from one end and with identifying marks at the other end. The strips are dipped in a buffer solution consisting of one part of 0·5 M oxalic acid solution and 10 parts of 0·1 M sodium oxalate solution, giving a *p*H of 3·5, the excess is blotted off, and the strips placed taut across a plastic carrier which rests upon a platform flanked on each side by an electrode trough filled with the same buffer solution; into these troughs dip the ends of the paper strips, the start line being to that side which is away from the positive pole, and the buffer content of the paper strips is equalized by the passage of a current for half an hour. The solution to be tested is then applied from a micropipette to the starting line, at the centre, and at each margin, and the current passed for a further half-hour. During this period, the borate ion will travel some 20 to 40 mm. towards the anode. The paper strips are then dried in the horizontal position at room temperature.

The detector reagent is prepared by leaving 1 g. of turmeric to stand in 100 ml. of acetone for 2 hours; this is then filtered, and to the filtrate are added 40 ml. of a saturated solution of oxalic acid in water and 10 ml. of concentrated hydrochloric acid. This detector is applied from an atomizer to each side of the paper so that it is well impregnated without any run-off; the paper is left under a hood to dry, the air being warmed if the humidity is relatively high. The red colour bands produced are proportional to the quantity of borate in the solution tested. It is stated that as little as 0·01 μg. of boron on the paper has been detected. A list of standards is given. The distance travelled by the borate is not linear with time, but in a given period of time it is linear with the voltage applied. Alkaline buffers give more colour, but acid buffers give a more rapid development of colour and the colour is less likely to fade with time. During iontophoresis of samples of urine, which was used untreated, it was constantly observed that in addition to the red boron–turmeric band a blue band of unknown origin was present farther out towards the anode. *M. A. Dobbin Crawford*

808. **Comparative Serum and Cerebrospinal Fluid Transaminase Levels in Acute Cerebrovascular Disorders**
M. MIYAZAKI. *Bulletin of the School of Medicine, University of Maryland* [*Bull. Sch. Med. Maryland*] **42**, 20–26, April, 1957. 5 refs.

A study is reported from the University of Maryland of the glutamic oxalacetic transaminase (G.O.T.) levels in the serum and cerebrospinal fluid (C.S.F.) in acute cerebrovascular disease. Control observations showed that in 30 patients without neurological or systemic disease, who were to receive spinal analgesia, the G.O.T. level in the C.S.F. was 2 to 30 units, and in 10 healthy volunteers the level in the serum was 22 to 36 units. A marked rise in the serum G.O.T. level in 3 patients with liver disease was not associated with a corresponding rise in the C.S.F. level, but serum and C.S.F. values estimated in 20 patients within 5 days of an acute cerebrovascular accident showed moderate rises. Of 37 patients with miscellaneous neurological conditions, 2 with hydrocephalus (congenital in one and suspected acquired after third ventricle tumour in one) and one patient with status epilepticus showed a rise in the C.S.F. level of G.O.T. *M. Sandler*

809. **Intraglobulin Fractional Analysis as an Aid in the Differentiation of Medical from Surgical Jaundice**
E. M. GREENSPAN and D. A. DREILING. *Gastroenterology* [*Gastroenterology*] **32**, 500–509, March, 1957. 7 figs., 18 refs.

As an aid to the differential diagnosis of jaundice of differing aetiology the changes in the pattern of the serum globulin fractions, which have been shown to have diagnostic significance, were studied by means of a series of four simple determinations, namely, the serum mucoprotein concentration as a measure of α_1 globulin, the acid precipitable globulin (A.P.G.) tubidity (for α_2 plus β globulin), the zinc sulphate (Z.S.) turbidity (for γ globulin), and the total bound polysaccharide value mainly as a measure of α globulins. The series consisted of 100 patients with hepatocellular jaundice and 60 with obstructive jaundice under treatment at the Mount Sinai Hospital, New York.

The results showed that a low serum mucoprotein value, low A.P.G. turbidity, high Z.S. turbidity, and a low A.P.G. : Z.S. turbidity ratio were associated with hepatocellular jaundice; thus a normal or high muco-

protein value, high A.P.G. turbidity, normal or low Z.S. turbidity, and a high A.P.G. : Z.S. turbidity ratio occurred in more than 95% of the cases of obstructive jaundice and in less than 10% of the cases of hepatocellular jaundice. Although these tests have certain drawbacks, which are discussed, they gave results which compared favourably with those obtained by estimation of cephalin flocculation, serum alkaline-phosphatase level, and other tests used in the differential diagnosis of jaundice, and they have the advantage of being simple enough for use in general clinical laboratories.

J. E. Page

810. **Serum Transaminase Activity: a Comparison of the Pyruvic and Oxalacetic Transaminases**

M. CHINSKY, R. J. WOLFF, and S. SHERRY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 400–408, April, 1957. 5 figs., 12 refs.

Because the increase in the serum oxalacetic transaminase level in acute myocardial infarction is not specific for this particular disease state, several workers have studied other enzyme systems. In this paper from the Jewish Hospital and Washington University School of Medicine, St. Louis, Missouri, is reported a comparison of serum oxalacetic transaminase activity with serum pyruvic transaminase activity in 150 patients with a variety of diseases. For the former the normal range was up to 40 units per ml. and for the latter it was up to 30 units. Values above 50 and 40 units respectively were regarded as high. The serum oxalacetic transaminase level was high in all 24 patients with myocardial infarction, but the pyruvic transaminase level was high in only 9 of them. With one exception the rise in the former was considerably greater than the rise in the latter. In 4 out of 5 cases of acute hepatitis serum pyruvic transaminase activity rose more than oxalacetic transaminase activity; in the remaining case the reverse was observed. Of 15 patients with cirrhosis of the liver, 10 showed an increase in the serum oxalacetic transaminase level and 6 an increase in the pyruvic transaminase value. There was a rise in both values in 3 out of 4 patients with acute interstitial pancreatitis.

The authors conclude that the serum pyruvic transaminase level is not uniformly more sensitive than the oxalacetic transaminase level as an indicator of hepatocellular damage. They suggest that determination of serum pyruvic transaminase activity may prove more useful in excluding the presence of hepatic necrosis.

C. L. Cope

811. **A Screening Test for Cystic Fibrosis of the Pancreas Using Analysis of Saliva**

W HART and M. J. NAIME. *Pediatrics* [*Pediatrics*] **19**, 372–376, March, 1957. 6 refs.

The authors describe a modification of the screening test for cystic fibrosis of the pancreas described by Silverman and Shirley (*Pediatrics*, 1955, **15**, 143; *Abstracts of World Medicine*, 1955, **18**, 180), in which the degree of absorption of an iodinated fat (" lipiodol ") is determined indirectly by measuring urinary iodide excretion. In the modified method the secretion of odide in the saliva, which is easier to obtain from very young children than urine, is measured. A dose of 0·5 ml. of lipiodol per kg. body weight is given by mouth mixed with honey, and saliva collected after 1, 2, 3, and 4 hours, either by expectoration into a clean tube or by aspiration with a pipette and rubber teat. Each sample is diluted serially to a maximum of 1:64 and 5 drops of 8N nitric acid and 3 drops of 1% starch solution added to each tube. A blue or purple colour is given if iodide is present in the saliva. The test can be simplified further by testing only the 1:16 and 1:32 dilutions of the 3- and 4-hour saliva samples.

The test was carried out at the Children's Mercy Hospital (University of Kansas School of Medicine), Kansas City, Missouri, on 30 children suffering from various diseases not related to the pancreas and on 11 children with proved fibrocystic disease. In the former group iodine was detected in the 3- or 4-hour saliva sample in a dilution of at least 1:8 in all cases. In the latter group iodine was detected only in dilutions of 1:2 or less, if at all. The results were unaltered when specimens of saliva were kept for 24 hours at room temperature.

M. Lubran

812. **Diphenylamine Reaction in Chronic Joint Diseases**

M. ADAM, J. MALECEK, and M. KŮTOVÁ. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 69–72, March, 1957. 16 refs.

The increased intensity of the purple colour reaction with Dische's diphenylamine reagent in the protein-free [?] filtrate of the patient's serum (the heterogenous mixture generally known as orosomucoid) is generally recognized as a feature of certain malignant and active inflammatory diseases, and has been regarded as an index of activity in rheumatic fever. The present paper, from the Institute of Rheumatic Diseases, Prague, analyses the findings of this reaction carried out on the serum of patients with chronic joint diseases, the results being compared statistically with those for estimation of the erythrocyte sedimentation rate, the non-glucosamine serum polysaccharide level, and the serum mucoprotein (orosomucoid) level. In 50 healthy control subjects the results showed no difference between the sexes. The test was then performed in 100 cases of rheumatoid arthritis (of which 50 were in Steinbrocker's Stage II, and 50 in Stages III and IV), in 50 cases of ankylosing spondylitis, and in 50 patients with degenerative joint disease. The spectrophotometric readings are given as optical density $\times 1{,}000$ at 530 mμ.

The mean for the controls was 0·311 (S.D. 0·024), the value of 0·350 being the upper limit in normal subjects. The mean for patients with ankylosing spondylitis was 0·354 (S.D. 0·041), the value being above the 0·350 level in 25 cases. Of the patients with Stage-II rheumatoid arthritis, for whom the mean was 0·419 (S.D. 0·096), 39 showed values above the 0·350 level. For those with rheumatoid arthritis of Stages III and IV the mean was 0·434 (S.D. 0·078), 42 showing values above the normal limit, while of those with degenerative joint diseases (mean 0·334 (S.D. 0·036)), 35 were within the normal limits. From the statistical evaluation the authors conclude that " the difference between the mean diphenyl-

amine reaction in second stage rheumatoid arthritis, on the one hand, and in degenerative joint disease and ankylosing spondylitis on the other, was highly significant. The difference in the erythrocyte sedimentation rate was not significant. Correlation between the diphenylamine reaction levels and non-glucosamine polysaccharide levels was significant at the 0·1 per cent level in all groups of patients . . . The authors deduce that the diphenylamine reaction may be used as a measure of the degree of inflammation not only in rheumatic fever, but also in rheumatoid arthritis and ankylosing spondylitis ".

[No reference is made to the fact that the diphenylamine reaction is considered to be due to sialic acid, which is dissociated from the protein complexes by the initial heating procedure, or to many reports that the ratios of polysaccharide and sialic acid levels to the protein tyrosine level are not necessarily always constant.]

Harry Coke

HAEMATOLOGY

813. **Leukocyte Agglutinins in Human Sera. Correlation between Blood Transfusions and Their Development**

R. PAYNE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 587–606, April, 1957. 1 fig., 39 refs.

The discovery of auto-antibodies for erythrocytes in patients with acquired haemolytic anaemia has suggested that such antibodies may be present for leucocytes in patients with leucopenia. At Stanford University School of Medicine, San Francisco, therefore, tests for leucocyte agglutinins were carried out on sera from 350 patients with some type of blood disorder and from 50 normal subjects. They were found in 38 of the patients but in none of the normal subjects. In 34 of the patients, there was a history of blood transfusion, and it was noted that multiple transfusions seemed to increase the risk of developing agglutinins. In the other 4 patients, who showed leucocyte agglutinins but had no history of blood transfusion, the agglutinins were atypical, in that they were not persistent and could not be demonstrated by all the tests at any one time.

Most of the patients in whom agglutinins were found suffered from anaemia of various types, leukaemia, idiopathic thrombocytopenic purpura, or one of the collagen diseases. There was no correlation between the presence of leucocyte agglutinins and that of leucopenia or neutropenia, and no patient's serum agglutinated his own leucocytes, so that no auto-immune activity can be postulated. The agglutinins acted as artificially induced iso-antibodies, but further blood transfusions were not followed by any anamnestic reactions. Of the 32 patients with leucocyte agglutinins of whom full details were available, 13 had experienced a transfusion reaction such as fever. The presence of leucocyte agglutinins did not correlate with the presence of the L.E. factor, erythrocyte antibodies, Rh antibodies, or platelet agglutinins.

[The paper includes a discussion and a valuable bibliography of this relatively new subject.] *T. B. Begg*

814. **The Serum Platelet Activity Test.** (Le test d'activité plaquettaire du sérum)

D. ALAGILLE and J. P. SOULIER. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét clin. biol.*] **2**, 231–246, March, 1957. 6 figs., 3 refs.

It has been demonstrated by O'Brien (*Brit. J. Haematol.*, 1955, **1**, 223), using the thrombin-generation test, that normal human serum has a platelet-like activity. The present authors, writing from the National Blood Transfusion Centre, Paris, point out that antithrombin interferes with this test, and they have therefore developed what they claim to be a more sensitive and specific test, based on the ability of normal and abnormal sera to improve the prothrombin consumption in recalcified platelet-free normal plasma. [The original paper should be consulted for full technical details.]

This test of serum " platelet activity " was performed on the serum of 204 patients suffering from various haemostatic defects. The activity was low in all of 49 cases of thrombocytopenia, in 13 out of 18 cases of thrombopathy of various types not accompanied by thrombocytopenia, and in 3 out of 4 cases of thrombocythaemia with impairment of platelet function, but it was normal in all 10 cases of thrombocythaemia in which tests of platelet function gave a normal result. The test result was abnormal in 5 out of 15 cases of Willebrand's disease and in 10 out of 36 cases of " haemophilia " of various types, but was normal in 5 patients receiving treatment with dicoumarol and in 15 cirrhotic patients who had an adequate number of platelets.

The authors discuss the physico-chemical properties of the platelet factor and suggest that it is probably identical with platelet Factor III, or platelet prothromboplastin. *T. B. Begg*

MORBID ANATOMY AND CYTOLOGY

815. **Morphology of Compensatory and Adaptation Processes in the Nervous System.** (Морфология компенсаторно-приспособительных процессов в нервной системе)

A. I. STRUKOV and S. K. LAPIN. *Архив Патологии* [*Arkh. Patol.*] **18**, 21–30, No. 8, 1956. 14 figs.

In the post-mortem study here reported from the First Moscow Medical School the changes in the central and peripheral nervous systems found on histological examination of necropsy material were classified as follows. (1) Those due to age, such as accumulation of lipofuscin, shrinking of nervous cells, and thickening of dendrites. (2) Reversible morphological manifestations of functional change, such as partial chromatolysis, acute swelling of nerve cells, and varicose swellings of nerve fibres. (3) Changes of a degenerative—and sooner or later irreversible—character, such as marked swelling of the nerve cells accompanied by total chromatolysis, karyolysis, or complete destruction of the whole cell, pyknosis, calcification, and fragmentation.

Besides these regressive changes, however, the authors describe a 4th group which they term " compensatory and adaptational " changes. These they believe to be

histological manifestations of functional regeneration in the nervous system, which appear to lead to a more or less complete reconstruction of the lesions caused by a great variety of diseases—the material studied came from cases of hypertension, chronic nephritis, tuberculosis, subacute endocarditis, pneumonia, bronchitis, asthma, whooping-cough, cancer, pemphigus, and others. These "progressive" changes included: (1) regeneration of nerve fibres and proliferation of the collateral fibres which tighten the network of interneuronal links; (2) hypertrophy of the body of the nerve cell caused by hyperfunction; (3) a compensatory increase in the number of nucleoli and nuclei in the nerve cells; (4) colonies and "symplasts" of nerve cells in the peripheral nerves, which they regard as the starting point of new nerve-cell formation; (5) an increase in the actual number of nerve cells by means of amitotic cell division; and (6) an increase in the number and size of argyrophil granules.

Experiments carried out by other workers are also quoted. These have shown an increase in the number of nerve cells containing two nuclei following stimulation of the superior cervical sympathetic ganglion on the corresponding side. *F. S. Freisinger*

816. **The Anatomical Appearance in Rheumatic Tricuspid Valve Disease**

A. HOLLMAN. *British Heart Journal* [*Brit. Heart J.*] **19**, 211–216, April, 1957. 7 figs., 12 refs.

To obtain information concerning the anatomy and function of the rheumatic tricuspid valve for use before subjecting a patient to tricuspid valvotomy the author, at University College Hospital, London, studied 21 specimens from cases of tricuspid-valve disease. Reviewing the literature he points out that the tricuspid valve is anatomically much weaker than the mitral valve as regards the prevention of incompetence, a point which was emphasized in his findings in the diseased valves. The mitral valve was found to be affected in all the cases (the aortic valve in 14), and this diseased mitral valve tended, in contrast to the tricuspid valve, to be further protected from incompetence by its large anterior cusp. Of the 5 valves showing well marked stenosis, 4 were considered to be incompetent also, while in 8 of the 16 showing slight or no stenosis there was probably considerable incompetence. The author found it difficult to see the fused commissures from the atrial aspect, so that presumably they would also have been difficult to palpate at valvotomy during life. *J. B. Wilson*

817. **Diffuse Endomyocardial Sclerosis**

J. B. LYNCH and J. WATT. *British Heart Journal* [*Brit. Heart J.*] **19**, 173–185, April, 1957. 7 figs., bibliography.

The clinical and pathological features of 4 cases of diffuse endomyocardial sclerosis which came to necropsy are discussed in this paper from the University of Liverpool. The main clinical findings were suggestive of a constrictive pericarditis, usually with eosinophilia or incompetence of the mitral and tricuspid valves. At necropsy the main pathological change consisted in marked fibrosis of the endocardium, the fibrosis extending into the inner third of the myocardium. There was little or no evidence of coronary arterial disease. The similarity of these findings to those in endomyocardial fibrosis in African natives and in congenital fibroelastosis in infancy is noted. Although the pathological changes in the former are similar to those in diffuse endomyocardial sclerosis, the changes in congenital fibroelastosis are so different that the two conditions must be considered as separate entities.

The aetiology of adult endomyocardial sclerosis is discussed, and the authors consider the most probable initial site is the subendothelial muscle, with subsequent endocardial thrombosis. These initial changes may have different causes, which in 2 cases may have been allergy and malnutrition respectively. *J. B. Wilson*

818. **The Hepatic Hilar Lymphatics of Man. Their Relation to Ascites**

A. H. BAGGENSTOSS and J. C. CAIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 531–535, March 21, 1957. 5 figs., 18 refs.

On the generally acceptable assumption that the predominant lymph flow from the liver is along the course of the hilar portal veins and bile ducts, the authors, at the Mayo Clinic, examined the lymphatics of the hilar region in necropsy specimens taken between clamps fixed at the duodenum and at the hilus. After the specimens had been fixed in formalin sections were cut, embedded in paraffin, and stained by the haematoxylin and eosin and the elastin H–van Gieson methods. Specimens were obtained from 100 consecutive routine necropsies on patients without ascites and from 28 necropsies on patients with ascites alone, 30 with ascites and cirrhosis, and 10 with cirrhosis but no ascites.

It was found that the mean number of lymphatics in the hepatoduodenal ligament was higher in patients with ascites and in those with cirrhosis, with or without ascites, than in routine necropsy cases in which ascites was absent. In cases of cirrhosis the lymphatic channels were not only dilated, but also had thickened walls, possibly because of increased lymphatic pressure.

B. G. Maegraith

819. **An Examination of Skin from Patients with Collagen Disease Utilizing the Combined Alcian Blue–Periodic Acid Schiff Stain**

E. P. CAWLEY, J. F. A. MCMANUS, C. H. LUPTON, and C. E. WHEELER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **27**, 389–394, Dec., 1956. 2 figs., 13 refs.

Fibrinoid alteration of collagenous tissue, so characteristic of the so-called collagen diseases, is known to be preceded by a local increase in concentration of acid mucopolysaccharides. Structures containing acid mucopolysaccharides are selectively stained by Alcian blue, a relatively new phthalocyanine dye. A method combining Alcian blue staining with the periodic-acid–Schiff technique was used by the authors in the examination of involved skin from 28 patients with various collagen diseases, the resulting excellent colour contrast facili-

tating the recognition of material stained by Alcian blue (A.B.-positive material).

Although approximately constant in the several specimens from each individual collagen disease under consideration, the quantity of A.B.-positive material varied from one disease to another. Small quantities of A.B.-positive material were present throughout the upper dermis in discoid lupus erythematosus, in the near vicinity of the small vessels of the upper dermis in morphea and generalized scleroderma, and throughout the upper dermis and in close proximity to damaged vessels in periarteritis nodosa. Small quantities of A.B.-positive material were also present throughout the upper dermis in normal skin. A.B.-positive material was remarkably abundant, by contrast, in the upper and middle dermis in dermatomyositis and disseminated lupus erythematosus.

[For details of the method of staining the original paper should be consulted.] *A. Swan*

820. **Comparative Studies on the Histo-pathology of Syphilis, Yaws, and Pinta**

C. M. HASSELMANN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] 33, 5–12, March, 1957. 18 figs., 31 refs.

The mass campaigns which have been undertaken in recent years against the treponematoses in many countries of the world have focused attention on the epidemiology, mode of transmission, clinical manifestations, and control of syphilis, framboesia tropica (yaws), and pinta. The author, who writes from the University of Erlangen but was formerly in charge of the World Health Organization Treponematosis Control Programme in Indonesia and the Philippines, considers that the different clinical lesions and modes of transmission of these three treponemal diseases are conditioned by the distinctive behaviour of the treponemes in the host's tissues.

In syphilis it is his opinion that the usual necrosis of the primary indurated papule leading to the typical hard chancre is due to the direct toxic reaction of *Treponema pallidum*. The epidermis proper shows only moderate acanthosis and spongiosis, while in the cutis infiltrations of round cells, fibroblasts, and histiocytes and occasional giant cells are found. In primary and secondary syphilis the conspicuous inflammatory changes are seen in the intima and media of capillaries with obliteration of the lumina. In yaws on the other hand the initial papule grows into a papilloma with exuberant inflammatory response in the epidermis and cutis. There is widespread acanthosis of the epidermis proper and the severe inflammatory changes seen in the corium and cutis attest to the acute response of these mesodermal parts. In the "plasmacytoma" the blood vessels are not affected, either in the initial papule or the metastatic polypapillomatous efflorescences, and the intima and media remain intact. It is suggested that only in late yaws does sudden necrosis with ulceration set in when sensitization has developed to such an extent that any sudden increase of antigen may enhance an apparent allergic exacerbation of the pre-existing skin lesions. In pinta the histo-pathological architecture is similar to that in yaws, but allergic exacerbation of existing skin pintides with ulcer formation never occurs. There is no vascular involvement at any stage.

The author concludes that the tendency of both yaws and pinta to affect the upper layers of the skin only, without affecting the cardiovascular or central nervous systems, is an example of "epidermotropism", in contrast to the involvement of the inner organs ("mesodermotropism" or "panblastotropism") which is typical of syphilis. Thus the different sorts of biological behaviour in the host largely explain the differences in the clinical and pathological features of these three diseases. *Douglas J. Campbell*

821. **Changes in the Gastro-intestinal Tract in Hypertensive Disease. (Gastro-intestinal Crises in Patients Suffering from Hypertension.)** (Об изменениях желудочно-кишечного тракта при гипертонической болезни (желудочно-кишечные кризы у больных гипертонией)

A. N. KOLTOVER. *Архив Патологии* [*Arkh. Patol.*] 18, 30–39, No. 8, 1956. 4 figs., 21 refs.

The post-mortem macroscopical and histological examination of the gastro-intestinal tract of 26 patients whose death was attributed to hypertension or its complications showed gross changes in 14 cases and marked microscopic changes in 7. In 12 cases the gross changes consisted in multiple acute ulcers—in the stomach of one of the patients no fewer than 10 ulcers were present. Less frequently (2 cases) chronic ulcers occurred, these being in the stomach and duodenum respectively. Some cases also showed infarcts in the small intestine. In the large intestine, however, neither ulcers nor infarcts were found, but on the other hand multiple haemorrhages occurred in all parts of the gastro-intestinal tract.

In the author's opinion these lesions were mainly due to microscopic vascular changes, such as plasmatic infiltration of the wall of the smaller vessels, occlusion of the lumen by a homogeneous protein-like mass, necrosis of the vessel wall, and perivascular infiltration; this last could, however, be easily differentiated from periarteritis nodosa, since it surrounded the vessel but did not infiltrate its wall, and consisted of fairly uniform round cells in contrast to the polymorphous character of infiltration in periarteritis nodosa. The changes—which frequently led to microscopic infarcts of the mucosa—were severest in the regions usually recorded as being under higher functional stress (that is, the lesser curvature of the stomach and the duodenum) and in the submucous layer of the stomach and intestine. No relation could be shown between the lesions described and changes in the central nervous system (such as haemorrhage or softening) or between the lesions and the occasional occurrence of uraemia. Emotional stress seemed to aggravate the lesions; for example, the patient with the 10 acute gastric ulcers died as the result of perforation of one of them immediately after a "crisis-like" sharp rise in the blood pressure caused by emotion. In several cases the lesions had caused repeated small haemorrhages with consequent anaemia. The author

concludes that gastro-intestinal changes in hypertensive disease occur much more frequently than is generally believed, since they easily escape clinical diagnosis.

[In the recent literature changes in the gastro-intestinal tract have been described in experimental hypertension in animals as well as in man, the reported incidence being between 7 and 15% of all cases of hypertension. In the present study, based on 26 cases only, the number of cases with gastro-intestinal changes seems to be extremely high, even if the cases described as showing "marked microscopic changes" are not taken into account.] *F. S. Freisinger*

822. **Electron Microscopic Investigations on Sections from Lymph Nodes and Bone Marrow in Malignant Blood Diseases**

H. Braunsteiner, K. Fellinger, and F. Pakesch. *Blood* [*Blood*] **12**, 278–294, March, 1957. 16 figs., 19 refs.

Sections of lymph nodes and specimens of bone marrow from patients with malignant lymphogranulomatosis, plasmacytoma, lymphosarcoma, and acute and chronic leukaemia were examined under the electron microscope.

Structures of particular interest observed in Sternberg cells of malignant lymphogranulomatosis are small dark "granular bodies" and "vesicular bodies". The former are present in large numbers and show a tendency to form clusters; they are found chiefly in cells rich in ribonucleoproteins. The vesicular bodies are also found in cells in material from patients with acute leukaemia; nothing is known of the function of these bodies. An organized ergastoplasm is to be seen in malignant plasmacytes from myeloma, in plasmacytoma, and in lymphoid cells from macroglobulinaemia, but not in acute leukaemia. Its development and its relation to protein production and secretion are demonstrated.

A. W. H. Foxell

823. **Hepatic Lesions in Sickle Cell Anemia**

Y. S. Song. *American Journal of Pathology* [*Amer. J. Path.*] **33**, 331–351, March–April, 1957. 11 figs., 20 refs.

The author, writing from the University of Tennessee, reviews the necropsy findings in 31 fatal cases of sickle-cell anaemia occurring between 1935 and 1955 in patients aged 3 months to 45 years.

In all cases the liver was enlarged and deep purple or mahogany red in colour. On microscopical examination the most prominent and constant feature was severe distension of the sinusoids by sickled erythrocytes. Phagocytosis by the Kupffer cells was not, however, a marked feature. Necrosis and atrophy of liver cells due to the sinusoidal obstruction were seen in most cases and were of varying extent, being most severe in the paracentral areas. Hyaline thrombi in the sinusoids were present in some cases, derived no doubt from the haemolysis of sickle cells. Thrombi in the hepatic arterioles and venous capillaries were also seen in a number of cases. In 7 of the cases there was fibrous proliferation in the peripheral zones, this probably representing healed massive necrosis, and in 9 there was advanced cirrhosis. The mechanism of causation of these liver changes is discussed. *R. B. Lucas*

824. **Lesions in Kidneys Removed for Unilateral Hematuria in Sickle-cell Disease**

F. K. Mostofi, C. F. V. Bruegge, and L. W. Diggs. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **63**, 336–351, April, 1957. 11 figs., 10 refs.

The authors report, from the Armed Forces Institute of Pathology, Washington, D.C., the findings in one renal biopsy specimen and in 21 kidneys removed for the treatment of unilateral haematuria. In 10 of these 22 cases sickling had been found on clinical investigation, while the remaining 12 presented an identical histological picture but haematological confirmation was lacking. Unequivocal sickling of erythrocytes in formalin-fixed tissues was seen in all cases; simple distortion by formalin is quite different from the true sickling observed here. Only prolonged exposure of the tissue to oxygen abolishes sickling. Haematological differentiation into cases of sickle-cell trait, sickle-cell anaemia, and haemoglobin S and C disease was not possible because of insufficient data, but collateral evidence suggested that these were all cases of sickle-cell trait.

The clinical details of these 22 patients, who were well developed young negro men not acutely ill, are presented in a table. Some had pain in the costovertebral angle over the affected kidney and all had haematuria (in 19 cases from the left kidney) which had been present for several days up to 2 years; in 10 cases there had been previous episodes. A transitory renal filling defect was seen on the radiograph in 15 cases. Nephrectomy was performed in 21 cases, in 7 as a life-saving measure because of profuse bleeding, and was followed by clinical recovery in all but one patient, who died in uraemia.

Macroscopically, the kidneys were swollen, but free from any of the lesions suspected in the various clinical diagnoses (which included tuberculosis, stone, pelvic ulceration, and neoplasm) and showed no gross alteration on the cut surface. Histologically, sickled erythrocytes were invariably present. The most striking change consisted in severe stasis of sickled erythrocytes in the peritubular capillaries of the cortex and medulla and extravasation of blood into the peritubular areas or the tubules, with separation of the tubular epithelium from the basement membrane. Older lesions showed partial or complete loss of tubular epithelium and iron pigment in the adjoining epithelial cells or in the stroma. Small areas of dense fibrosis, with or without hyalinization, were seen in the medulla in 20 cases. Focal papillary engorgement was noted in 14 cases, oedema producing a myxomatous appearance to the papillary stroma in 19, and subepithelial papillary haemorrhage in 10 cases. Further changes, occurring in a few cases each, were observed in the papillae, collecting tubules, and renal pelvis.

The authors state that the basic lesion in these cases is the stasis of sickled erythrocytes which results from the increased viscosity of blood containing them. This

is followed by ischaemia, infarction and perivascular oedema, exudation, and haemorrhage, the end-stage being necrosis, fibrosis, and atrophy. There is thus no indication for nephrectomy and it should be avoided.

F. Hillman

825. **The Renal Lesion in Epidemic Hemorrhagic Fever** J. OLIVER and M. MACDOWELL. *Journal of Clinical Investigation* [*J. clin. Invest.*] **36**, 99–223, Jan., 1957 (Part 2). 63 figs., 31 refs.

The authors describe and discuss the renal findings in 35 fatal cases of epidemic haemorrhagic fever (E.H.F.) which occurred in Korea during 1952–3. A preliminary survey of the tissues was made after fixation in formalin or Zenker's solution and staining with haematoxylin and eosin. Later, the material was stained by the Masson, acid-fast green, and other techniques. Microdissection of nephron systems was carried out on many preparations [the results of which are demonstrated in a series of beautiful and brilliant photographs and camera lucida drawings]. Disturbances of renal function do not occur in the initial febrile stage of the illness, but may occur in any subsequent stage, most commonly in the hypotensive phase which follows the febrile, but also in the successive phases of established oliguria, diuresis, and convalescence.

In the febrile stage renal clearances are high, indicating normal or increasing renal blood flow. As the hypotensive stage develops evidence of damage to capillary blood vessels appears and the haematocrit and serum protein values rise, indicating loss of fluid from the circulation. Heavy proteinuria develops. This stage may precipitate into acute vascular failure or pass on to a transition state in which the haematocrit value falls and the plasma volume rises, indicating the return of fluid to the circulation. In this stage also fatal (transition) shock may appear. In the hypotensive phase death from primary shock accounts for one-third of the fatalities.

During the hypotensive phase, which lasts 2 days or so, renal clearances are depressed and the urinary output is irregularly reduced. Changes occur in the blood flow through the kidney which are most noticeable in the subcortical zone of the medulla, where there is intense engorgement despite the reduction in flow. At this stage in this region there is a " solid mass of entrapped cells " in the affected vessels, through the walls of which plasma escapes and causes some intertubular oedema. So far there is no haemorrhage, but early changes appear in both the cortical and medullary portions of the proximal convolutions. The lesion at this stage is still reversible.

The transitional period is ushered in by the appearance of haemorrhage into the congested subcortical zone. This becomes more marked, progressive, and infiltrative in the next stage, which is characterized by established oliguria and structural and functional renal changes which are irreversible. The nephrons are destroyed in in the middle half, the injury equally involving proximal tubules, ascending and descending loops, and collecting tubules. The serious damage is confined to the areas of congestion and haemorrhage and so appears mostly in the medulla, or in the cortex in regions where there has been cortical extension of the circulatory disturbances. Factors involved in this tubular destruction are the physical pressure from vascular distension and, more important, anoxia from the congestive stasis. Post-obstructional dilatation is found in some parts of the tubules (including the ascending loops) above the subcortical zones of pressure. The authors provide a very satisfactory explanation of this bewildering post-obstructional dilatation by pointing out (with excellent illustrations) that the human kidney contains nephrons which actually turn within the cortex and never reach the medulla. Glomerular filtrate can flow through these to the point of origin of the collecting system and thence to the distal portions of neighbouring nephrons connected to it. It is clear from this dilatation that although the tubules are interrupted at this stage, the circulation in the glomeruli is continuing. Hence in the early hypotensive phase in which no such dilatation occurs reduction of urinary volume results from changes in circulation only, whereas in the stage of established oliguria compression and destruction of tubules are the important factors. The renal lesions in the diuretic phase are similar. Later, healing becomes evident in the formation of scar tissue containing remnants of the damaged nephrons. The explanation of survival in non-fatal cases which have developed renal changes lies apparently not in repair of damaged nephrons, but in the escape of great numbers of nephrons from irreversible damage.

The authors sum up as follows. " In general, the mechanisms of the two variations in urinary output, oliguria and diuresis, are similar in EHF to those which operate in the classical example of Acute Renal Failure associated with various forms of traumatic or toxic injury. In both, a decrease and subsequent restoration of renal blood flow would seem to be immediate factors in the production of decreased and augmented urine flow. As accessory mechanisms that reduce tubule flow in both forms of renal damage, increased intra-renal tension from interstitial edema or swelling of osmotic origin of the epithelium of the proximal convolutions must be considered, and any ' casts ' that may be present must act as deterrents of tubular flow. In contrast to these similarities between the nature and causes of decreased urinary output in Acute Renal Failure and EHF one difference has been previously noted; the *establishment* of the oliguria in the latter. Though the factors which establish the oliguria, tubular disruption, are present in all forms of ischemic renal damage, the concentration of its obstructive effect by a zone of subcortical hemorrhage is present only in EHF. The sudden onset of diuresis, at times from no urine excretion to over several liters in 24 hours, makes it certain that a circulatory phenomenon is concerned and not the restitution of some structural element.

" It would seem possible to resolve this apparent anomaly and rationalize our metaphor by the recognition that the renal lesion in EHF is Acute Renal Failure in an individual whose peripheral vascular bed, including the renal, is atonic and permeable as a result of an infectious disease."

[This is one of the most interesting and careful studies published over the last decade on the problems of acute renal failure. The stress laid by the authors on the vascular and anoxic elements in the pathogenesis of the condition confirms the aptness of the abstracter's original label of "renal anoxia" for similar renal failures (*Lancet*, 1945, **249**, 578).] *B. G. Maegraith*

826. **Nephrotic Glomerulonephritis**
D. B. JONES. *American Journal of Pathology* [*Amer. J. Path.*] **33**, 313–329, March–April, 1957. 11 figs., 22 refs.

This paper from the State University of New York, Syracuse, presents an account of the finer details of structure of the glomeruli in nephrotic glomerulonephritis. The kidneys from 20 cases of the disease were examined, the main staining method used being the periodic-acid–silver-methenamine technique; this technique gives similar results to the periodic-acid–Schiff method, but with much greater contrast.

In nephrotic children dying of intercurrent infection early in the disease, glomerular changes amount to little more than a slight increase in connective-tissue cells in the glomerular stalk, though the tubules show marked fatty changes. In those in whom the nephrotic syndrome is complicated by azotaemia, however, there are definite glomerular changes, as shown by an increase in connective tissue in the centre of each glomerular lobule and some thickening of the pericapillary basement membranes. Some of the capillaries may be partly blocked by lipid-filled cells. Tubular atrophy and dilatation are very marked at this stage.

The more advanced lesions are seen in older children and adults. These are characterized by large glomeruli, the lobules of which are distended by cellular scar tissue. In the early stages of the lesion the capillaries are patent, but later they become obliterated and only nodular masses of scar tissue remain. Although the lesion resembles in some respects that of diabetic glomerulosclerosis, it is differentiated from that condition by the absence of extensive hyaline arteriolar sclerosis of the afferent arteriole, the well developed cellularity of the scars, the uniform involvement of all glomeruli, and the marked capillary obliteration. The author designates this type of lesion "chronic lobular glomerulonephritis". Another type of lesion is the membranous form of nephrotic glomerulonephritis, in which there is hyaline thickening of the basement membranes about the glomerular capillaries. There is some increased cellularity of the glomeruli and often the capillary lumina are narrowed by the thickened walls. *R. B. Lucas*

827. **Adenomatous Polyps of the Large Intestine. Pathology and Histogenesis**
A. VALDES-DAPENA and W. J. BECKFIELD. *Gastroenterology* [*Gastroenterology*] **32**, 452–461, March, 1957. 7 figs., 12 refs.

Between June, 1949, and June, 1954, at the Graduate Hospital of the University of Pennsylvania, Philadelphia, a total of 171 polyps of the large intestine were removed and examined; in addition 150 of 288 specimens resected for carcinoma were examined, polyps being found in 46. Most of the polyps in the former group were in the terminal segment of bowel, 85% being in the sigmoid or lower colon and none in the ascending colon, hepatic flexure, or caecum. On the other hand 17 of the 46 polyps found incidentally were in the right colon.

A series of 37 minute mucosal nodules were studied in detail, 6 of which could be classified as adenomata. No visible evidence of glandular proliferation was found in 7 of the 37 specimens. Early changes were seen in the cells in 7 of the remaining 30; these changes being "presumably in the direction of less function and greater reproduction". In 23 specimens there was visible increase in cellularity, with branching of the glands where this increase was most marked. In the early stages the development of a connective-tissue stalk tended to overshadow the adenomatous component. Only 2 of 3 small lesions showed evidence of inflammation in the lamina propria.

The authors consider that in the genesis of a polyp there may be a primary epithelial alteration which is capable of producing a reactive nodular swelling of the submucosa. This later develops into a fully fledged pedicle. When the epithelial proliferation fails to elicit this stromal reaction no pedicle is formed. The importance of this lies in the fact that malignant change in such a sessile lesion leads to early deep invasion. A relatively short pedicle probably indicates a rapid growth rate on the part of the adenomatous component and a more aggressive character. *A. W. H. Foxell*

828. **Adenomatous Polyps of the Appendix in Children**
T. K. SHNITKA and R. W. SHERBANIUK. *Gastroenterology* [*Gastroenterology*] **32**, 462–474, March, 1957. 5 figs., 29 refs.

Appendicular polyps are rare, only 40 to 60 cases having been recorded in the literature. The authors of this paper from the University of Alberta, Edmonton, Canada, present 4 cases of appendicular polyp in children, the polyps being of the adenomatous type in 3 and of the lymphoid type in one. The adenomatous polyps showed the characteristic features of the "childhood" polyps found in the large intestine, with dilated, cystic glandular spaces, certain epithelial changes, abundant fibrous-tissue stroma, and inflammation. These childhood polyps are neoplastic lesions which are susceptible to inflammation and may give rise to mild symptoms, when surgical removal may be necessary. Malignant change has rarely been observed in the adenomatous type. The authors state that the one case of lymphoid polyp was included to represent the group of non-epithelial polyps of the appendix, and "corresponds to similar lesions in the large intestine; the polyp was undoubtedly produced by the inflammatory changes of suppurative appendicitis".
A. W. H. Foxell

829. **The Identification and Clinical Significance of Casts**
G. E. SCHREINER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 356–369, March, 1957. 23 figs., 29 refs.

Microbiology and Parasitology

830. **The Microcultural Behaviour of Alveolar Cells and *Pneumocystis carinii* in the Interstitial Plasma-cell Pneumonia of Infants.** (Das mikrokulturelle Verhalten von Alveolarzellen und von *Pneumocystis carinii* bei der interstitiellen plasmacellulären Säuglingspneumonie)
G. PLIESS. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **68**, 153–184, 1957. 10 figs., bibliography.

After an exhaustive survey of the literature [the bibliography contains 260 references] the author reports his own thorough investigations, carried out at the Pathological Institute of the University of Hamburg, on *Pneumocystis* pneumonia. These included the examination of imprints, sections, and microcultures of alveolar contents in hanging-drops, in microchambers, and on micro-agar plates on microscope slides. Original preparations and cultures were examined by transmitted light, dark-field illumination, and phase-contrast microscopy after fixation and staining by various methods.

The appearances and the transformations undergone by the cellular contents of the alveoli and of *Pneumocystis* masses are described. The majority of these transformations are considered to be the result of post-mortem autolysis, but the possibility of autolysis *in vivo* is stressed. Of particular interest is the observation of new formation of cysts in microcultures. An important distinction is made between the " matrix phase " and cyst formation, it being the latter which causes the " honeycomb " appearance characteristic of sections of the lung in this disease. [And as the abstracter has observed on two occasions, the matrix phase may be greatly predominant over the cyst forms.] In the cyst form the author distinguishes: (1) the envelope, (2) the matrix, and (3) the granules. The granules, which are Feulgen-positive [and which the abstracter has described as granules of protozoal chromatin] are identical in the cyst form and in the matrix phase.

In regard to staining properties, the author stresses that the thick-walled cysts only are Gram-positive, and warns against drawing chemical or taxonomic conclusions from the appearances with the Gram or Gridley stains. He discusses changes of cyst granules in microcultures and the possibility of their confusion with bacterial inhibition forms. *H. S. Baar*

831. **The Microcultural Behaviour of Yeasts and Bacteria in the Interstitial Plasma-cell Pneumonia of Infants.** (Das mikrokulturelle Verhalten von Hefezellen und Bakterien bei der interstitiellen plasmacellulären Säuglingspneumonie)
G. PLIESS. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] **68**, 185–204, 1957. 5 figs.

Using the same methods as those described in the previous paper [see Abstract 830] the author studied the changes occurring in microcultures of yeasts and bacteria from 14 cases of *Pneumocystis* pneumonia and 3 control cases. The organisms were isolated and identified in macrocultures. Apart from " pneumocystoid " transformations, the appearance in two hanging-drop microcultures of yeast cells which stained red with Giemsa's stain is remarkable. However, there was no structural correlation between these " pneumocystoid transformations " and *Pneumocystis carinii*, and in preparations from 9 cases of *Pneumocystis* pneumonia there was no growth of yeasts.

The author questions the conclusions drawn from the experimental production of " pneumocystoid " structures in rats after the aspiration of yeasts because similar structures were seen without yeast aspiration in young rats treated for a long time with cortisone and " supracillin ". Bacteria showed inhibition forms, multiplication of granules, coccoid transformation of rods, cysts, and bacterial conglomerates which vaguely resembled *Pneumocystis*, but on no occasion were structures seen identical with the cyst forms of *Pneumocystis carinii*.
H. S. Baar

832. **A Critical Examination of a Simple Method of Isolating Tubercle Bacilli from Sputum**
A. J. O'HEA. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **173**, 389–398, 1957. 7 refs.

A comparative study is reported from the University and Western Infirmary, Glasgow, of the customary method of concentrating sputum with 4% sodium hydroxide and the swab method described by Nassau. In the latter two sterile swabs mounted on orange sticks are moistened in distilled water and rotated in the sputum so that a portion of the sputum adheres to the swab. Each swab is then immersed in 5% oxalic acid at room temperature for 25 minutes and then in 5% sodium citrate for 10 minutes to neutralize the acid. A Löwenstein–Jensen slope is inoculated from each swab, and incubated at 37° C. for 8 weeks.

Specimens of sputum were examined for acid-fast bacilli before and after concentration with sodium hydroxide. Comparison of the results with those obtained by the swab method showed that the latter was very efficient with specimens containing a large number of tubercle bacilli, and in such cases was preferable to the sodium hydroxide technique, because the risk of infection through the release of a heavily contaminated aerosol (as may happen with a method involving centrifugation) was minimized. The sodium hydroxide method, however, gave a higher proportion of positive results with specimens containing few tubercle bacilli. *John M. Talbot*

833. **The Growing Prevalence of Drug Resistance among Tubercle Bacilli, and Its Assessment**
J. E. TINNE. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 245–248, June, 1957. 2 figs., 15 refs.

834. **Studies on the Development and Persistence of Complement-fixing and Neutralizing Antibodies in Human Poliomyelitis**

E. H. LENNETTE and N. J. SCHMIDT. *American Journal of Hygiene* [*Amer. J. Hyg.*] **65**, 210–238, March, 1957. 3 figs., 15 refs.

The titres of complement-fixing and neutralizing antibodies were determined in 69 patients with poliomyelitis (4 with the non-paralytic form of the disease) at various intervals during the 2 years following onset of the illness, the study being carried out at the Viral and Rickettsial Disease Laboratory, Berkeley, California. In 51 patients from whom poliomyelitis virus was isolated, homotypic complement-fixing antibody was slower in appearing and in reaching the maximum level than was homotypic neutralizing antibody. The maximum complement-fixing antibody levels were variable, both in degree and rate of attainment, but had been reached in all the patients by the third month after the onset of the illness. After the peak these titres declined, and at the end of 2 years only 22 of the 41 patients with a Type-I infection had demonstrable complement-fixing antibody. Of those who lost antibody completely, 15 did so within a year of infection.

The titre of homotypic neutralizing antibody was high in the majority of patients shortly after the onset of the illness and was considerably higher than the complement-fixing antibody titre in the same patient. Although the neutralizing antibody titre declined from the peak over the 2-year period, complete loss was not observed in any of the patients with Type-I infection.

Complement-fixing antibody to Type-II virus was encountered in 5 and neutralizing antibody in 12 of the patients with Type-I infection. Antibody against Type-III virus was found in 15 by the complement-fixation test and in 16 by the neutralization test. The tests did not always provide definitive information concerning the type of infecting virus, but a diagnosis of poliomyelitis was "established" by the complement-fixation test in approximately 65% of the patients as compared with 40% by the neutralization test". *A. Ackroyd*

835. **The Use of Erythrocyte Sensitizing Substance in the Diagnosis of Leptospiroses. I. The Sensitized Erythrocyte Agglutination Test**

D. E. MCCOMB, D. J. W. SMITH, D. L. COFFIN, R. A. MACCREADY, and R. S. CHANG. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **6**, 90–100, Jan., 1957. 7 refs.

The extraction of erythrocyte-sensitizing substances (ESS) from 5 strains of leptospira has previously been described (Chang and McComb, *Amer. J. trop. Med. Hyg.*, 1954, **3**, 481). These substances are capable of sensitizing erythrocytes, rendering them agglutinable by specific leptospiral antiserum. The present communication reports further studies, including the extraction of ESS from other leptospiral serotypes, and the application of the agglutination test in the diagnosis of human leptospiroses. The strains investigated comprised *Leptospira icterohaemorrhagiae, L. canicola, L. pomona, L. autumnalis, L. sejroe, L. hebdomadis, L. grippotyphosa, L. pyrogenes, L. bataviae, and L. ballum.* ESS were extracted from all except *L. grippotyphosa*, although sera from rabbits immunized by this strain agglutinated erythrocytes sensitized with ESS from the other nine strains. Sodium taurocholate was used for the extraction of ESS, and after isolation they were titrated by comparison with a known positive serum with human Group-O erythrocytes.

The sensitized erythrocytes were prepared by mixing 1 part of 10% erythrocyte suspension with 10 parts of a diluted preparation of ESS containing at least 4 units per ml. The agglutination test was carried out by mixing the washed sensitized erythrocytes with various dilutions of the serum under examination.

The loss of activity of ESS preparations preserved with 1·3% formalin, with 0·02% thiomersalate, and without preservative and kept at 0° to 4° C. was studied. After 4 weeks' storage all had suffered some diminution of activity, but after 13 weeks the two with preservatives maintained a consistently higher level than the preparation without preservative. Even after 41 weeks the preparation containing formalin still had one-quarter of the original strength.

The antibody titres of human leptospiral sera determined by means of the sensitized erythrocyte agglutination (S.E.A.) and agglutination lysis (S.E.L.) tests were compared, the latter, with one or two exceptions, giving much higher values. These tests were carried out on sera from patients with confirmed or suspected leptospirosis and from dogs with or without the disease.

It was found that the antibody against ESS deteriorates on storage at −20° C. for more than 12 to 18 months and disappears from the blood rather rapidly after convalescence from infection. However, good correlation between the results of the S.E.A. and S.E.L. tests was obtained with fresh sera. *Edward Hindle*

836. **The Use of Erythrocyte Sensitizing Substances in the Diagnosis of Leptospiroses. II. The Sensitized Erythrocyte Lysis Test**

R. S. CHANG, D. J. W. SMITH, D. E. MCCOMB, C. F. SHARP, and J. I. TONGE. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **6**, 101–107, Jan., 1957. 8 refs.

The results are reported of the examination by the S.E.A. and S.E.L. tests [see Abstract 835] of sera from 40 proved cases of human leptospiroses occurring in Australia. The diagnosis was confirmed in all 40 cases and the group specificity of the tests were shown by the ability of *Leptospira pomona* ESS to detect human infection caused by *L. icterohaemorrhagiae, L. canicola, L. pomona, L. hyos, L. australis* A., *L. australis* B., and the "Robinson", "Kremastos", and "Celledoni" strains. Sheep erythrocytes were found to give greater sensitivity than human erythrocytes in the S.E.L. test, but not in the S.E.A. test. *Edward Hindle*

837. **A Quantitative Leprosy Complement Fixation Test.** [In English]

W. A. COLLIER and E. GEHR. *Documenta de medicina geographica et tropica* [*Docum. Med. geogr. trop. (Amst.)*] **9**, 165–168, June, 1957. 3 figs.

Pharmacology

838. **Antiemetic Properties of a New Chlorphenothiazine Derivative, Proclorperazine**

D. G. FRIEND and G. A. MCLEMORE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 732–735, May, 1957. 6 refs.

Chlorpromazine is a potent anti-emetic except in motion sickness, for which hyoscine and some antihistaminics, such as cyclizine, are superior. The antiemetic properties of prochlorperazine, a derivative of chlorpromazine with the side-chain found in cyclizine, were studied at the Peter Bent Brigham Hospital (Harvard Medical School), Boston. The drug was given to 25 patients with a wide variety of diseases by mouth or intramuscular injection in a dosage of 10 mg. every 4 to 6 hours or in a suppository in a single daily dose of 50 mg. There was complete control of nausea and vomiting in 14 and of vertigo in one with Ménière's syndrome. In 10 patients vomiting was controlled but some nausea persisted; the response in the remaining 2 patients was poor. In an additional patient with Ménière's syndrome without nausea and vomiting severe vertigo responded promptly. With a daily dose of 60 mg. or more drowsiness was common. Higher doses caused confusion, dizziness, and faintness in some patients, but in this small series no serious toxic effects were encountered. *Derek R. Wood*

839. **Clinical Evaluation of a New Oral Nonmercurial Diuretic**

B. WAINFELD, J. J. YARVIS, and A. FRANKHAUSER. *Circulation* [*Circulation (N.Y.)*] **15**, 426–429, March, 1957. 8 refs.

The administration of mercurial diuretics has two drawbacks—the occasional toxic effects and, in most cases, the inconvenience and pain of repeated injections. A safe oral diuretic would therefore have obvious advantages. Preliminary studies with "mictine" (aminometradine) suggested that this drug might possess the necessary properties. A group of 24 patients with heart disease who had been attending the out-patient department of the Kings County Hospital Center, Brooklyn, N.Y., and who had had at least one weekly injection of a mercurial diuretic for 6 months were selected for the trial. Their need for a diuretic was confirmed during the 4 weeks immediately preceding the trial, when the mercurial diuretic was withdrawn.

Aminometradine was given in doses of 0·8 to 1·6 g. daily, depending on the response. Administration on 3 consecutive days each week was found most effective, and if the tablets were taken with food gastric disturbance was avoided. None of the patients, however, could tolerate more than 1·6 g. daily. No toxic effects and no changes in blood chemistry were observed. The observation period was 6 months. Two patients failed to derive any benefit from the drug and 17 became resistant, although later they responded to another derivative of pyrimidinedione. In 5 cases the good response was maintained during the 6-month trial period.

The authors conclude that aminometradine "deserves a trial in cases of moderate congestive failure and in all cases where mercurial diuretic therapy is contraindicated". *F. Starer*

840. **The Effect of Disulfiram on the Action and Metabolism of Paraldehyde**

M. L. KEPLINGER and J. A. WELLS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **119**, 19–25, Jan., 1957. 3 figs., 10 refs.

The effect of disulfiram on the duration of paraldehyde-induced hypnosis in mice has been studied at the Northwestern University School of Medicine, Chicago. Paraldehyde in doses of 0·75 or 1 g. per kg. body weight was administered intraperitoneally or orally in 5% aqueous solution and disulfiram in doses of 25 to 800 mg. per kg. either intraperitoneally or orally as a suspension in 20% acacia solution.

In one series of experiments the effects of different doses of disulfiram given by different routes 5 hours after the intraperitoneal injection of paraldehyde at two different dose levels on the mean sleeping time of groups of 10 mice each were studied. In another the effect of 200 mg. of disulfiram on the sleeping time of groups of mice given 0·75 g. of paraldehyde 0·25, 0·5, 3, 5, and 24 hours later was studied, while in a third series the effect of 200 mg. of disulfiram per kg. on the toxicity of paraldehyde given 5 hours later in various doses orally and peritoneally was determined.

It was found that either 50 mg. of disulfiram per kg. intraperitoneally or 200 mg. of disulfiram per kg. orally prolonged the sleeping time of mice given paraldehyde intraperitoneally; the effect was evident when the paraldehyde was given within 15 minutes of the disulfiram injection, increased to an apparent maximum when it was given 5 hours later, and disappeared within 24 hours. Disulfiram had no effect on the toxicity of paraldehyde given intraperitoneally, but increased its toxicity slightly when the paraldehyde was given by mouth and was thus more slowly absorbed. This appeared to support the hypothesis that disulfiram acts by retarding the metabolism of paraldehyde. Comparison of the blood levels of paraldehyde and acetaldehyde in dogs that had received paraldehyde by stomach tube before and after the administration of disulfiram also supported this hypothesis, while the fact that high blood levels of acetaldehyde were maintained in association with those of paraldehyde indicated that disulfiram primarily retards the breakdown of acetaldehyde and suggested that an equilibrium exists in the body between paraldehyde and acetaldehyde. In this way the removal rate for paraldehyde, and thus the persistence of its effect, could be related to the existing level of acetaldehyde and, in turn, to its rate of metabolism. *J. E. Page*

Chemotherapy

841. **Combined Effects of Antibiotics and Radioactive Phosphorus on Bacteria *in vitro*.** (Комбинированное действие на бактерии антибиотиков и радиоактивного фосфора в пробирочных опытах)
M. A. TUMANYAN. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 14–18, No. 1, Jan.–Feb., 1957.

Radioactive phosphorus incorporated in culture media in concentrations of 30 to 50 μc. per ml. does not in itself affect the growth of bacteria, but when combined with an antibiotic, such as penicillin or streptomycin, it enhances the bacteriostatic and bactericidal effect of the antibiotic on *Escherichia coli*, dysentery bacilli, and staphylococci. Streptomycin and radioactive phosphorus added to hard culture media in concentrations which do not prevent the growth of dysentery bacilli inhibit the development of the colonies and favour the appearance of R colonies. *A. Orley*

842. **Cortisone–Thyroid Therapy of Metastatic Mammary Cancer**
H. M. LEMON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 457–484, March, 1957. 6 figs., bibliography.

At the Massachusetts Memorial Hospitals, Boston, 30 unselected cases of metastatic mammary carcinoma were treated for periods of 10 days to 37 months with cortisone or cortisol. Reports in the literature have shown that in nearly all cases of breast cancer there are also pathological changes in the ovaries, thyroid, adrenal glands, or hypophysis, the commonest being stromal hyperplasia in the ovarian cortex, and it is thought that this may account for the oestrogen production that sometimes persists in postmenopausal women with breast cancer. There is evidence that exogenous corticoid suppresses secretion of sex hormones by the adrenal cortex, though such treatment has no effect on, or may even increase, ovarian oestrogen secretion. For these reasons the author performs oophorectomy on all patients under 65 years of age before instituting corticoid treatment; he points out that above this age remissions may be obtained with cortisol despite the presence of the ovaries. The dosage of the corticoids was 200 to 300 mg. daily for 1 or 2 days and 50 to 100 mg. daily thereafter. With higher doses there is the danger of causing Cushing's syndrome and also the metabolism of excess corticoid to androgen and oestrogen. Desiccated thyroid (15 to 120 mg. daily) was given to most of the patients after 4 to 8 weeks' treatment with corticoid in order to overcome the thyroid-depressant action of the latter.

The 30 patients are analysed on the basis of age, clinical condition, degree and site of metastasis, and ovarian status. Objective improvement (manifested by gain in weight, return of normal physical activity, survival, decrease in urinary calcium excretion, repair of bony metastases or reduction in size of soft-tissue metastases, and/or decrease in the serum acid-phosphatase level) occurred in 18 of the 29 patients treated for more than one month, but this improvement was only temporary in most cases. However, in 10 cases it lasted for more than 6 months, and one patient is still in remission after 37 months' treatment, but only 7 are still alive. Patients with ovarian stromal hyperplasia seemed to respond better than those without. The patients subjected to oophorectomy usually had a recurrence of hot flushes after several weeks' treatment, this often coinciding with remission. Gonadotrophin excretion (assayed on the mouse uterus) was usually increased during treatment. In at least 3 of these cases no benefit was obtained until the supplementary treatment with thyroid extract was instituted. *Peter C. Williams*

843. **A *Lactobacillus* Preparation for Use with Antibiotics**
D. GORDON, J. MACRAE, and D. M. WHEATER. *Lancet* [*Lancet*] **1**, 899–901, May 4, 1957. 7 refs.

On the assumption that the intestinal side-effects which frequently occur during the oral administration of antibiotics are due to partial destruction of the natural intestinal flora the authors have investigated the value of " enpac ", a preparation of antibiotic-resistant strains of *Lactobacillus acidophilus* combined with nutrient factors, in young patients under treatment at Ham Green Hospital, Pill, Bristol, for streptococcal respiratory infections or scarlet fever. All the patients, aged 1 to 13 years, received tetracycline, 10 mg. per kg. body weight daily for 5 days, and in addition half of them (Group 2) were given 3 g. of enpac four times daily for 9 days. Bacteriological examination of the stools was carried out at intervals throughout the trial.

The results showed: (1) an initial increase in the faecal staphylococcal count in both groups, followed by a significant fall in Group 2, but a continued rise of tetracycline-resistant staphylococci in the patients given the antibiotic alone; (2) a reduction in the number of lactobacilli in the faeces in Group 1, but a rapid and persistent increase of resistant strains of these organisms in Group 2; (3) an increase of enterococci in both groups during treatment, with a return to pre-treatment levels a week later; (4) no apparent relationship between the number of coliform bacteria present and antibiotic administration; and (5) no significant alteration in the growth of yeasts. It is concluded that enpac can check the increase of potentially pathogenic staphylococci. Clinically, no intestinal or other side-effects occurred in either group. *Gerald Sandler*

844. **The Sensitivities and Cross Resistances of Gram-negative Bacilli to Antibiotics**
B. A. WAISBREN and C. L. STRELITZER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 744–750, May, 1957. 21 refs.

Infectious Diseases

845. **Isolation of the Virus and the Complement-fixation Reaction in the Diagnosis of Influenza.** (Virus-Nachweis und Komplementbindingsreaktion in der Influenza-Diagnostik)
J. JOCHIMS, E. SCHOMERUS, W. BREDOW, and H. LIPPELT. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] 82, 497–499, April 12, 1957. 12 refs.

This paper describes investigations carried out on a group of children admitted to hospital during an epidemic of influenza B in Germany during the period January to March, 1955. In 12 cases throat garglings or washings were sent by post overnight packed in ice and salt for examination at the Institute of Tropical Medicine, Hamburg. Influenza virus Type B Lee was isolated in 3 cases, demonstrating the practicability of this method of transmission. The specimens were obtained during the first 3 days of the illness.

Serial specimens of serum taken at intervals of at least a week were tested by means of the complement-fixation test against influenza virus Type A_1 or Type B Lee, an increase in titre to more than 1:20 being taken as a positive result. Control specimens from 15 children admitted with other diseases about 5 months after the outbreak of the epidemic gave negative results. The complement-fixation titre was raised initially in 3 children admitted with typical influenza. In serum from 45 other children probably suffering from influenza there was a significant increase in titre against Type B in 8 cases. In 2 cases there was also a positive titre against Type A_1 at the 13th day, but this fell later, while the Type-B titre rose. *M. Lubran*

846. **Mumps Virus and Subacute Thyroiditis. Evidence of a Causal Association**
E. EYLAN, R. ZMUCKY, and C. SHEBA. *Lancet* [*Lancet*] 1, 1062–1063, May 25, 1957. 3 figs., 2 refs.

Subacute thyroiditis is usually regarded as rare, but the authors report that a comparatively large number of cases have occurred in Israel in the past few years. The initial symptoms are a mild pyrexia, pain in the neck radiating to the ears which is worse on swallowing, and, a few days later, swelling of the thyroid gland. Tachycardia, sweating, and a tendency for the eyes to stare were often seen, and some patients complained of abdominal pain. There was slight leucocytosis and an increase in the serum plasma-bound iodine level (above 8 μg. per 100 ml.), and the erythrocyte sedimentation rate was raised. In contrast the uptake of radioactive iodine was greatly reduced in 12 out of 15 cases. Treatment with cortisone or ACTH (corticotrophin) resulted in rapid resolution of the condition.

Since it seemed probable that the disorder was due to a virus infection, complement-fixation tests against the mumps virus were carried out and gave a positive result in 10 out of 11 cases. From this finding and control studies the authors concluded that a titre of 1:80 or more is evidence of recent contact with mumps infection. A virus was isolated from a biopsy of the thyroid gland in 2 of the cases, and animal passage and agglutination tests showed it to be identical with the mumps virus. When these cases occurred there was a high incidence of mumps in Israel and 4 of the later patients had had recent close contact with mumps. *Winston Turner*

847. **Present Indications for Cortisone Therapy in Acute Viral Hepatitis**
R. S. NELSON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 685–695, April, 1957. 5 figs., 8 refs.

In the great majority of patients with viral hepatitis the prognosis is excellent. Whatever favourable effects cortisone may have on the course of the disease, it is not therefore indicated in the average case. Occasionally, however, the course of the disease is unfavourable and acute hepatic failure threatens, and it is in such cases that the author advises cortisone therapy. Amongst the indications for the use of this hormone which he suggests are a serum bilirubin level of over 15 mg. per 100 ml.; nausea, vomiting, and anorexia uncontrolled by intravenous infusion of glucose; and in particular any insidious change in mentality which may herald hepatic coma.

Five case histories are presented from the Brooke Army Hospital, San Antonio, Texas, to illustrate how the manifestly downhill course of an acute viral hepatitis may be favourably altered by cortisone therapy. All cases showed immediate clinical improvement, but equally striking was the prompt reduction in serum bilirubin level, in 2 cases amounting to 30 mg. per 100 ml. In one case there was a clinical relapse and a sharp rise in serum bilirubin level when cortisone dosage was lowered too quickly, but control was regained immediately the dose was increased. The dose of cortisone always appeared to be large, and occasionally courageous dosage in the region of 1 g. daily was used to initiate therapy. *J. N. Harris-Jones*

848. **The Treatment of Epidemic Hepatitis with Prednisolone.** (Zur Behandlung der Hepatitis epidemica mit Prednisolon)
W. SIEGENTHALER and G. ZUBER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **87**, 315–317, March 30, 1957. 2 figs., 11 refs.

This paper from the Kantonsspital, St. Gallen, Switzerland, describes the results of the treatment of 25 cases of infective hepatitis with prednisolone, 13 of the patients being men and 12 women. A control group of 8 men and 17 women were also observed for comparison, and the results are also compared with those in a previous series of 25 cases treated with cortisone or hydrocortisone. The patients' ages in the present series ranged from 25 to 81 (average 50·4) years and in the control group from 9 to 71 (average 38·5) years. The daily dose of prednisolone was 30 mg. (compared with

100 mg. of hydrocortisone in the previous series), the duration of the course being 10 days.

Subjective improvement occurred in all patients after 1 or 2 days' treatment and they had more appetite than those in the control group. Objective findings included a more rapid fall in the serum and urinary bilirubin levels in the treated patients than in the controls, though the serum albumin level and results of liver function tests [not detailed] returned more slowly to normal. There appeared to be little difference between the effects on the disease of hydrocortisone and prednisolone, but the low incidence of side-effects makes the use of the latter preferable. No case of hepatic coma occurred during this series.

[In a disease of self-limiting type such as infective hepatitis it is difficult to appraise the value of any treatment. In the abstracter's view the authors have not made out a convincing argument in favour of steroid therapy for this disease.] *I. M. Librach*

849. **Osteo-articular Sites of Brucellosis**

J. Rotés-Querol. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 63–68, March, 1957. 30 refs.

At the University Medical Clinic, Barcelona, 174 cases of brucellosis due to *Brucella melitensis* were studied during the period 1927–55. The diagnosis was based upon a history of exposure to infection, the presence of systemic symptoms, and the finding of positive results in various laboratory tests, such as blood culture. Of the 174 patients, 130 men and 44 women, signs of osteo-articular disease were detected in 148, being noted in 89% of males and 67% of females. The locomotor system was more often affected in patients over the age of 50. Myalgia occurred in only 5·7% of the cases. In one patient with a subcutaneous nodule on the anterior aspect of the tibia biopsy examination revealed changes similar to those observed in the brucellar granuloma. Some patients had cellulalgia, suppurative cellulitis, or tendinous synovitis, and 3 had acute bursitis.

In 86 cases osteophytes were detected in the peripheral joints. Changes in the joints ranged from transient effusion to severe arthritis of 2 to 8 months' duration. Melitococcal sacro-iliitis occurred in 65 cases, being usually observed during the first month of the illness. Spondylitis affected 93 patients, especially elderly males; the signs and symptoms included pain in the vicinity of several vertebrae, rigidity of the back, and contracture of the paravertebral muscles. Radiological examination revealed focal lesions of the vertebrae, destructive lesions in the epiphysial region, and erosion of the anterior and lateral surfaces of the vertebral bodies. Complications included osteomyelitis of the spine and meningomyelitis. At necropsy granulation tissue was found in the bone marrow and trabeculae. Reconstructive lesions were detected in cases which had reached the subacute stage, and degenerative lesions were also detected in the vertebral bodies and intervertebral disks.

No cases of rheumatoid arthritis or ankylosing spondylitis were seen. Treatment consisted in rest in bed and administration of oxytetracycline and dihydrostreptomycin with sulphaguanidine. *A. Garland*

850. **Clinical Variants of Lambliasis.** (Клинические варианты лямблиоза)

I. A. Pavlyuchenko and S. K. Al'. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **35**, 76–80, No. 2, Feb., 1957.

While lambliae are often saprophytic, they may in some cases be pathogenic, and in such instances the symptoms are multiform. The authors report their findings and conclusions in 150 cases in which lambliae were found in the duodenal contents on one or more occasions and describe four clinical variations.

(1) In 64·8% of the cases the symptomatology was similar to that of chronic gastritis: nausea, eructations, heartburn, constant pain in the epigastrium or right hypochondrium aggravated by acid, fatty, or coarse foods, poor appetite (especially for fatty foods), and furred tongue. The liver margin was palpable, smooth, but not tender; as a rule the spleen was not palpable.

(2) In 12·6% of cases the symptoms suggested a duodenitis or even duodenal ulcer; indeed, a barium meal often showed a deformity of the duodenal cap. The symptoms did not respond to treatment for peptic ulcer alone, but did so after treatment with "acrichin" ("mepacrine"). If the symptoms were combined with those of cholangiitis, however, this treatment had to be reinforced with "syntomycin" [a Russian tetracycline preparation].

(3) In 10% of cases the pain was in the right iliac fossa, and these patients had in many cases been subjected to appendicectomy without relief. When the operation specimen was available to the authors, histological examination showed either sclerosis of the submucosa and infiltration with lymphoid cells or no inflammatory changes at all. This confirmed the reports of Klein and his associates, who found lambliae in 11 out of 17 appendices so removed, but no inflammatory changes. The authors consider that appendicectomy is not justified in cases of chronic appendical pain associated with lambliasis until the latter has been treated without relief.

(4) In 4% of cases the symptoms were those of enterocolitis, with dull pain, at times becoming violent, usually in the lower half of the abdomen, and distension, retching, vomiting, and diarrhoea (up to 10 stools a day). Ulceration may occur in such cases.

In 36% of all cases the free acid content of the gastric juice was reduced and in 22% free acid was absent. Of 27 cases of achlorhydria, the gastric juice in 8 became normal after treatment of the lambliasis. In 16% of the cases the antitoxic function of the liver was disturbed, and in 17% there was urobilinuria.

Treatment consisted of 3 courses of acrichin, each lasting 7 to 10 days, alternating with syntomycin or sulphonamide preparations. [The dosage is not specified, but in another article on lambliasis in the same journal a loading dose of 0·3 g. followed by 0·1 g. 3 times daily is mentioned, the loading dose being administered through a duodenal tube.] It is reported that 65% of the patients were cured, 31·7% relieved, and 3·3% unrelieved. These last were patients with symptoms of duodenitis together with cholangiitis, which are the most resistant to treatment. *L. Firman-Edwards*

Tuberculosis

851. **Tuberculosis among University Students: a 35 Year Experience**
J. A. MYERS, R. E. BOYNTON, and H. S. DIEHL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 201–217, Feb., 1957. 1 fig.

From 1920 to 1955 7,530 out of 155,021 students and members of the staff were referred to the chest clinic of the University of Minnesota Students' Health Service. Pulmonary tuberculosis was diagnosed in 1,055 cases, pleural effusion in 115, and extrathoracic tuberculous lesions in 61. During the first part of this period, when the medical examination undergone by all students entering the university was physical only, it was not unusual for cases of extensive chronic pulmonary tuberculosis to be missed until they revealed themselves by such symptoms as haemorrhage. In 1929 fluoroscopic examination of the chest was added to the routine procedure, since when between 3 and 4 times as many cases of tuberculosis have been detected on entrance. In addition, since 1931, *x*-ray film inspection has been carried out on all students who were tuberculin-positive on entrance, leading to the detection of further cases. The tuberculin test was introduced as part of the entrance examination of all students in 1928. Whereas in that year the number of tuberculin reactors amounted to about 33%, by 1945 the proportion had decreased to 6·4%. The influx of students after the second world war and after the Korean campaign, however, brought about an increase in the proportion of positive reactors, which has since fluctuated between 10 and 20%. This is attributed, in part, to " many having been in countries where little has been done to control tuberculosis ". Students who are tuberculin negative on entrance are subjected to 6-monthly retesting, and those showing conversion are given periodic physical and *x*-ray examinations. The methods of controlling tuberculosis among students of the School of Medicine have been particularly effective. Of those graduating between 1919 and 1932, 92 developed tuberculous lesions before or after graduation, of whom 11 died, whereas during the last 14 years only one student has developed a lesion large enough to be detected radiologically. In addition to cases of the clinical reinfection type of pulmonary tuberculosis, a considerable number of cases of primary disease have been observed, particularly among medical and nursing students. In these patients the disease was no different from that seen in childhood, the infiltrates resolving regardless of the amount of treatment given and no case of immediately progressive primary pulmonary tuberculosis being seen.

No form of immunization has been introduced, the authors preferring " to protect students by managing tuberculosis as a contagious disease ". They argue that as an attack of tuberculosis does not produce a reliable immunity, B.C.G. vaccination would destroy the value of the tuberculin test for control purposes without providing more certain protection. *Franz Heimann*

852. **The Tuberculin Reaction during Chemotherapy for Pulmonary Tuberculosis**
S. SCHWARTZ. *Diseases of the Chest* [*Dis. Chest*] **31**, 286–298, March, 1957. 12 refs.

The changes in the tuberculin reaction during chemotherapy for active pulmonary tuberculosis were investigated in 49 adult male patients being so treated at the Veterans Administration Hospital, Augusta, Georgia, who were tuberculin tested before the start of treatment and then at monthly intervals for the first 4 months and therafter bi-monthly up to one year. The test was carried out with 0·002 mg. of P.P.D. tuberculin which was given intradermally into the flexor aspect of both forearms; two diameters of the subsequent area of induration were then measured at right angles on the two arms and the mean of the 4 readings taken as the size of the reaction.

A significant increase in the size of the reaction area was present 1 to 2 months after the start of chemotherapy, the increase being especially marked in the group of patients receiving streptomycin and PAS, and also in patients under 50 years of age, those with advanced disease, and in Negro patients; the most significant increase occurred in 9 patients who originally had had an induration area less than 5 mm. in diameter. In most cases after the 2nd month the tuberculin reaction decreased and was least about the 8th month of treatment. No significant difference in the reaction in groups receiving different regimens of chemotherapy was demonstrated. *G. M. Little*

853. **Cyanacetic Acid Hydrazide Combined with Terramycin in the Treatment of Genito-urinary Tuberculosis.** [In English]
K. O. OBRANT and A. LIND. *Urologia Internationalis* [*Urol. int. (Basel)*] **4**, 16–24, 1957. 2 figs., 18 refs.

Nine patients with genito-urinary tuberculosis were treated with cyanacetic acid hydrazide (CAH) at the rate of 0·1 g. 4 times a day. In all cases but one the CAH treatment was combined with terramycin 1 g. a day in order to prevent the development of resistance to CAH. Thus a combined treatment against tuberculosis was carried out without including PAS, streptomycin or INH [isoniazid].

Laboratory investigations showed that terramycin does not impair the activity of CAH *in vitro*. Four patients had never had antituberculous chemotherapy and conversion of the urine was obtained in all these 4 cases.

Five patients, all with advanced renal tuberculosis, had been treated for years with PAS, streptomycin, conteben or INH without achieving conversion of the urine. One of these patients got allergic disturbances and the CAH treatment had to be stopped after only a month. In all the four other cases conversion was achieved and there have been respectively 11, 14, 14 and 19 negative guinea-pig tests since.—[Authors' summary.]

Venereal Diseases

854. **Prolonged Survival of *Neisseria gonorrhoeae*: an Aid to the Diagnosis of Gonorrhoea**

C. B. G. COLQUHOUN and G. N. COOPER. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 413–415, March 30, 1957. 3 refs.

The authors discuss methods and difficulties of diagnosis of gonococcal infections under conditions in Australia, where, it seems, cultural methods have been available only in clinics equipped for bacteriological investigation and have given inconsistent results. With a view to finding a satisfactory technique they investigated the possibility of the use of Stuart's holding medium (*Brit. med. J.*, 1948, **2**, 421; *Abstracts of World Medicine*, 1949, **5**, 353) as an aid to the routine cultural diagnosis of genital infections in males and females. The study lasted for more than a year and led to the conclusion that the method was satisfactory for the diagnosis and exclusion of gonococcal infection. Of 327 cases of gonorrhoea (out of 1,159 cases tested) in the male, smears and cultures were positive in 280 (85·5%), smears were positive and cultures negative in 34 (10·5%), and smears were negative and cultures positive in 13 (4%). Of 47 cases (out of 275 cases tested) in the female, smears and cultures were positive in 28 (59·5%), smears were positive and cultures negative in 2 (4·5%), and smears were negative and cultures positive in 17 (36%). The cultural method detected some 30% more cases in the female than direct microscopical examination, and for this purpose the Stuart technique proved of outstanding value. In males the method was less satisfactory, but gave useful confirmation of diagnosis obtained by smear examination. Relative lack of success with men was attributed to contamination of the specimens with *Proteus vulgaris* in some cases, to the collection of superficial and therefore oxygenated pus in others, and, perhaps most important, to the fact that some patients, especially seamen, had received self-administered treatment before presenting for diagnosis. *A. J. King*

855. **Occurrence of Late Syphilis in Untreated Syphilitic Patients**

J. TOWPIK. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 2–4, March, 1957. 2 figs.

Since the second world war the introduction in Poland of modern methods of venereal disease control has reduced the incidence of syphilis from 50 per 10,000 of the population in 1947 to 0·97 in 1955. In further efforts to discover untreated cases and thus lower the high incidence of latent syphilis so prevalent in Poland mass serological examinations and antenatal and pre-employment blood tests were carried out at the Institute of Dermatology and Venereology, Warsaw. These revealed 4,500 patients with different forms of late syphilis during the years 1950 to 1955. Of these, 500 patients aged from 26 to over 65 who had not been treated previously were selected for further analysis.

It was found that 164 (33%) had latent syphilis, while 234 (47%) had neurosyphilis, 91 (18%) cardiovascular syphilis, and 9 (2%) had late benign syphilis [2 being thus unaccounted for]. Males predominated in the groups with neuro- and cardiovascular syphilis while females predominated in the small group of latent and late benign syphilis; in 70 cases (14%) two forms of the disease coexisted. Of 26 married couples presumably infected with the same strain of organism, in only 5 instances did the disease take a similar course. In 38 cases showing advanced clinical signs of neurological involvement the cerebrospinal fluid was normal. In most of the neurosyphilitic patients active pathological processes had died out spontaneously at a comparatively early age. The author suggests that this analysis reveals the importance of individual immunological processes, the comparatively early development of systemic changes, and the frequency of the coexistence of more than one form of systemic change in untreated cases of syphilis.

Douglas J. Campbell

856. **Reiter Protein Complement Fixation Test for Syphilis**

G. R. CANNEFAX and W. GARSON. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **72**, 335–340, April, 1957.

A complement-fixation test for syphilis is described in which the antigen used is a protein fraction of the Reiter treponeme. This is prepared in bulk by growing the organism in Brewer's medium from which the agar has been removed and 10% rabbit serum added. After incubation for 4 to 6 days at 37° C. the organisms are separated by centrifuging and washed 3 times in saline to free them from constituents of the medium. Each gramme of sedimented organisms is resuspended in 20 ml. of saline and the treponemes broken down by freezing to −70° C. and thawing at 37° C., these processes being repeated 15 times. The suspension is centrifuged and the opalescent supernatant fluid containing the liberated protein separated off. The deposit is resuspended in 10 ml. of saline and subjected to 5 further cycles of the treatment outlined. The supernatant fluids are pooled and dialysed against ammonium sulphate solution in concentrations increasing from 10 to 75% of saturation. The protein which is precipitated is dissolved in 2 ml. saline for each original gramme of treponemes (wet weight) and dialysed against normal saline for 96 hours. After centrifuging, the supernatant constitutes the antigen. [It is not stated whether it is further diluted before use.] All the procedures of centrifugation and dialysis are carried out in the cold.

Tests were carried out by the Kolmer one-fifth-volume technique with the Reiter protein as antigen (R.P.C.F. test) in parallel with the treponemal immobilization (T.P.I.) test and the treponemal complement fixation (T.P.C.F.) test of Portnoy and Magnuson (*J. Immunol.*, 1955, **75**, 348; *Abstracts of World Medicine*, 1956, **19**,

442). The specificity of the R.P.C.F. test was assessed by examining 615 sera giving negative T.P.I. and T.P.C.F. reactions during a serological survey of an area with a high incidence of syphilis. These patients were presumed to be non-syphilitic, no clinical details being available at the time of testing. Sera from 14 of them were reactive with the R.P.C.F. test, and inquiry showed that 7 had previously been diagnosed as syphilitic and treated, while 3 denied any past history of the disease; no information could be obtained about the remaining 7 patients. A further 765 sera came from patients previously diagnosed as syphilitic. [It is not stated whether these were treated or untreated cases.] All stages of the disease were represented. The proportions of positive reactions given by the three tests were: T.P.I. 75·4%, R.P.C.F. 82·6%, and T.P.C.F. 86·8%. The inclusion of 140 patients with primary and 117 with secondary syphilis accounts for the low sensitivity of the T.P.I. test, as the appearance of immobilizing antibody is known to be delayed. Differences in sensitivity between the three tests with sera from the later stages of syphilis were not thought to be significant.

It is concluded that the R.P.C.F. test compares favourably in sensitivity and specificity with the T.P.I. and T.P.C.F. tests and that it merits further investigation.

A. E. Wilkinson

857. **Investigations on the Reproducibility of the Quantitative *Treponema pallidum* Immobilization Test.** [In English]

H. A. NIELSEN. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **40**, 119–135, 1957. 3 figs., 20 refs.

An investigation of the reproducibility of the quantitative treponemal immobilization (T.P.I.) test is reported from the State Serum Institute, Copenhagen. Two serum mixtures were studied, each consisting of equal parts of 6 human sera, and so prepared that Mixture A had a lower content of immobilizing antibody (immobilizin) than Mixture B. Mixture A contained serum from 3 cases of treated early syphilis, 2 cases of treated latent syphilis, and one case of treated congenital syphilis, while Mixture B contained serum from 3 cases of treated symptomatic syphilis, one case of treated and one case of untreated latent syphilis, and one case of untreated early syphilis. Altogether 32 pairs of titrations of the immobilizin content of the 2 mixtures were carried out over a 4-week period. The suspension of treponemes used was made up in basal medium (less thioglycollate) in two different batches, each divided into 8 portions. Each batch was then further subdivided into two groups, each group of 4 portions being made up with a different thioglycollate solution. It was estimated that the standard deviation of duplicate titrations of the same pool using the same complement and the same suspension of treponemes was 22% and that the standard deviation of repeated titrations of the same pool using the same complement but different suspensions was 52%. The contribution to the difference due to the use of varying suspensions of treponemes was about two-thirds of the total difference.

R. R. Willcox

858. **Experiences with a Follow-up Examination of 200 Tabetic Patients.** [In English]

T. ORBÁN. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **32**, 89–102, 1957. Bibliography.

The author presents the results of a follow-up study of 200 tabetic out-patients attending the National Dermato-Veneropathological Institution, University of Budapest, since 1952. Many of these had previously been treated in venereal and neurological clinics, up to 1949 with standard courses of bismuth and arsphenamine, and since then with penicillin, and 58% of them had minimal symptoms, with none of the typical tabetic complaints. The author considers this to be a general feature of treated neurosyphilis at the present day. The conclusions drawn from this study [which are in general agreement with British and American views] are that the best prophylaxis against tabes in the pre-penicillin era was at least four courses of arsenic and bismuth begun in the early seronegative stage of syphilis. Nowadays it is considered that penicillin in a total dosage of 12 to 18 mega units affords optimum treatment for this type of neurosyphilis, and that such treatment will often improve symptoms, even in cases shown to be inactive by cerebrospinal-fluid examination. When symptoms persist after treatment the author gives no further penicillin, but has found that vitamins, chlorpromazine, ACTH, vasodilator drugs, and atropine are all useful in appropriate cases.

G. L. M. McElligott

859. **Lymphogranuloma Inguinale in the Male in Liverpool, England, 1947 to 1954**

C. D. ALERGANT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 47–51, March, 1957. 1 fig., 16 refs.

A study is reported of 55 cases of lymphogranuloma venereum seen at Newsham General Hospital, Liverpool, during the period 1947–54. The patients were of many different nationalities and in all cases the infection appeared to have been acquired abroad, the majority in the East and 8 in Brazil; only 4 of the patients were infected in Europe—two in Portugal, one in Spain, and one in Italy. In view of admitted repeated exposures to infection in many cases the incubation period could be determined only approximately; it ranged from one to 14 weeks, and was from 2 to 6 weeks in the majority (of 45 cases).

A history of a primary sore was obtained in 13 cases (23%), but with one exception all the patients presented with inguinal or femoral buboes. Constitutional symptoms were absent or slight and complications were rare. In 11 of the cases other veneral conditions were present, the most common being latent syphilis. Of 14 cases of a doubtful or positive Wassermann reaction with no clinical evidence of syphilis, 8 (16·6%) were thought to represent biological false positive reactions and 6 to be due to latent syphilis. In the early part of the study the treponemal immobilization test was not yet available, and for diagnostic purposes the Frei intradermal test and the complement-fixation test (C.F.T.) were used as routine procedures. Titres of 1 in 20 or over were

found in 53 out of 54 C.F.Ts, whereas the Frei test gave a positive result in only 35 out of 51 cases. Moreover, there appeared to be no correlation between the titre with the C.F.T. and the Frei test, negative Frei-test reactions being found with C.F.T. titres as high as 1 in 320, and low titres of 1 in 20 being found in cases giving strongly positive reactions in the Frei test. Although it is generally held that in lymphogranuloma inguinale the Frei test becomes positive earlier than the C.F.T., the results of this study emphasize the superiority of the C.F.T. over the Frei test in the diagnosis of early cases. A complement-fixation test was performed on the cerebrospinal fluid in 5 cases, but with negative results.

The prognosis in lymphogranuloma venereum in the male is considered to be uniformly good, the course being benign as a rule with few complications. Sulphathiazole (1 g. 4 times daily for 10 to 14 days, repeated if necessary after one to 2 weeks' rest) was the drug of choice, while aureomycin was reserved for more obstinate or complicated cases. No relapses were seen, although in most cases the Frei test was still positive after treatment and the C.F.T. titre remained at its original level.

A. J. Gill

860. **The Effect of Antibiotics upon the Course of Non-gonococcal Urethritis**

C. E. LAIDIG and P. BERG. *Journal of Urology* [*J. Urol. (Baltimore)*] 77, 457–466, March, 1957. 20 refs.

Non-gonococcal urethritis (N.G.U.) is a common condition among U.S. service men in the Far East, and although several workers have already attempted to evaluate various therapeutic regimens, the follow-up period in most reported series has been too short. In this paper from a U.S. Air Force hospital near Tokyo the authors analyse the results of 10 weeks' treatment of 252 cases of venereal N.G.U. by four different methods: (1) of 49 patients treated with 1 g. of streptomycin and 4 g. of sulphadiazine daily for 4 days, 37 (76%) were cured; (2) of 60 patients given 1 g. of aureomycin daily for 4 days, 42 (70%) were cured; (3) of 63 patients treated with 3 tablets of the mild analgesic "pyridium" daily for 3 weeks, 49 (81%) were cured; and (4) of 80 patients given inactive placebo tablets for varying periods, 67% were cured.

Although the ultimate clinical outcome of the condition was the authors' main concern, the course of the disease in the various treatment groups was carefully watched and noted and their conclusions regarding its natural history, management, and treatment are valuable. They consider N.G.U. to be a low-grade, generally self-limited, inflammatory process typified by periods of complete remission followed by subsequent relapse, and that approximately two-thirds of the cases clear spontaneously without antibiotics. They found, however, that although a single course of antibiotics shortened the course of the attack in most cases it cured no greater number of patients than placebos or pyridium, and also that when additional therapy, usually antibiotics, was given to the patients who did not get well in a few weeks the eventual cure rates in all groups were substantially the same.

G. L. M. McElligott

861. **Treatment of Non-gonococcal Urethritis with Novobiocin**

R. R. WILLCOX. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] 33, 52–53, March, 1957. 2 refs.

A total of 42 previously untreated cases of non-gonococcal urethritis were treated at St. Mary's Hospital, London, with novobiocin, a new "wide-spectrum" antibiotic derived from *Streptomyces niveus* or *Strep. spheroides*. Two cases were subsequently found to have gonococci present and were therefore excluded. Of the 40 patients (24 white and 16 negroes) remaining, 20 received 1 g. of novobiocin daily divided in four doses for 6 days (total 6 g.) and 20 received 2 g. daily also for 6 days (total 12 g.). The incubation period ranged from one day to 28 days. Trichomonads were sought in 27 cases, but were found in none.

The follow-up schedule consisted in weekly observation for one month, including examination of two prostatic smears, and thereafter each month for a further 2 months, again with prostatic-smear examination. No attempt was made to distinguish relapse from re-infection. As the results were equally poor with both treatment schedules (6 g. and 12 g.) they were considered together. Among the 36 cases followed up for at least 7 days there were only 16 successes as against 20 failures, most of the latter being cases of non-response with persistent urethral discharge from the start. Comparison with previous series treated under similar conditions with other antibiotics showed that the failure rate with novobiocin (55·6%) was nearest to that obtained with only a placebo (68·2%). Toxic effects were few, only 2 patients having moderate gastro-intestinal upsets. It is concluded that novobiocin is ineffective in the treatment of non-gonococcal urethritis.

A. J. Gill

862. **Treatment of Non-gonococcal Urethritis**

E. E. PREBBLE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] 33, 43–46, March, 1957. 8 refs.

The lack of specific treatment for non-gonococcal urethritis and the modern tendency towards the lavish use of various antibiotics have prompted the author to protest against the high cost of such treatment and to warn against the possibility of creating drug resistance by its indiscriminate use in a condition in which the morbidity is low. These considerations have led him to compare the results of antibiotic treatment and of the old method of urethral irrigations. Because the majority of patients with non-gonococcal urethritis seen at the Liverpool Royal Infirmary were seamen the observation period was unavoidably limited to 15 days. Of 70 cases treated with erythromycin, 200 mg. 6-hourly for 5 days, 28 (40%) were considered to be failures; and of 93 cases treated with streptomycin, 1 g., together with sulphathiazole tablets, 1 g. 4 times daily for 5 days, 22 (24%) were failures; whereas of 73 cases treated with urethral irrigation with mercury oxycyanide solution, 1 in 8,000, once daily for 3 to 7 days, only 11, or 15%, were failures. The results help to confirm the author's view that treatment by irrigation is more rational than the haphazard use of antibiotics and worthy of trial in appropriately equipped clinics.

V. E. Lloyd

Tropical Medicine

863. **Plants as Aetiological Factor in Veno-occlusive Disease of the Liver**
G. BRAS, D. M. BERRY, and P. GYÖRGY. *Lancet* [*Lancet*] 1, 960–962, May 11, 1957. 6 figs., 29 refs.

The occurrence of veno-occlusive disease of the liver in children in Jamaica has been attributed to the use by the natives of " bush-tea ", a decoction of the leaves of various plants, as a remedy for ailments, and this theory is supported by the occurrence of a similar disease in cattle. Hepatic lesions have been produced in animals by feeding with *Senecio* (ragwort) and experiments are now reported in which 5 calves were fed on *Crotalaria fulva* (rattle box) and hepatic biopsies performed at monthly intervals. Four calves died without significant hepatic lesions, whereas the fifth developed obliterative changes in the hepatic veins after 6 months. The 5 control animals remained healthy. Photomicrographs of sections of the hepatic lesion in the fifth calf are reproduced, together with photomicrographs of sections of lesions in the liver of a horse fed on *Senecio erraticus barbaraefolius*. The similarity of these lesions to those seen in human veno-occlusive disease of the liver is stressed. Hepatic cellular damage has been reported in animals after feeding with these plants, and it is possible that more than one toxin is present, each with a different " target area ". *W. H. Horner Andrews*

864. **Self-healing, or Abortive, and Residual Forms of Childhood Leprosy and Their Probable Significance**
C. B. LARA and J. O. NOLASCO. *International Journal of Leprosy* [*Int. J. Leprosy*] **24**, 245–263, July–Sept., 1956 [received April, 1957]. 11 refs.

The authors describe the results of a study of 287 children born of leprous mothers at the Culion Sanitarium, Philippines, since 1932, and who showed some of the lesions of leprosy. Apparent complete healing occurred in 77·7%, incomplete healing in 12·5%, and progression of the infection in 9·7%. The most reliable finding on which to base the prognosis was the morphology of the lesions: thus the tendency towards healing was strongest in the papulo-nodular forms and other definitely circumscribed thickened lesions, was somewhat less in the weal-like and raised or flat macular lesions, and least in the infiltration-like, more or less diffusely thickened lesions. The lower the bacterial content of the lesion and the stronger the Mitsuda reactivity, the greater the tendency to heal. Histologically, healing occurred earlier in cases showing undifferentiated round-cell or monocytic infiltrates than in those with tuberculoid structure (except those with the papulo-nodules). Any relapses were usually seen in less than 3 years of apparent healing, and never occurred after 10 years. Relapses were more common in cases which began with a tuberculoid histology than in those with undifferentiated lesions, and they were also more frequent in cases with weal-like and macular types of early lesion than among cases with papulo-nodular, lichenoid, or scar-like indurated lesions. A small number of apparently healed cases continued to show minimal signs of active disease such as enlarged or tender nerve trunks with or without anaesthesia and micropapular or follicular residules at or near anaesthetic atrophic scars. Such cases are probably benign, but may become acute and be mistaken for new cases; they may also provide unrecognized foci for further spread.

Two other groups of children, each of 110 individuals, have been followed up since 1938. One group received intracutaneous injections of lepromin and the other served as a control group; both groups continued to be exposed to infection. There were indications that the group treated with lepromin derived some benefit from the injections, but the evidence is inconclusive. It is concluded from these observations that when a certain number of cases of leprosy are discovered during a survey it is probable that the population surveyed includes three times as many persons who have had the infection and who have recovered. *F. Hawking*

865. **Glomerular Filtration Rate and Renal Plasma Flow in Cholera and Acute Gastro-enteritis**
S. BANERJEE and H. GHOSH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **94**, 668–670, April, 1957. 7 refs.

In cholera, assessment of kidney function is of importance to predict prognosis, to learn the progress of the disease, and to suggest treatment. With this in mind the authors, working at Presidency College, Calcutta, India, have determined the glomerular filtration rate (by the inulin clearance test) and renal plasma flow (by the *para*-aminohippuric acid clearance test) in 14 patients with cholera, in 6 with acute gastro-enteritis, and for comparison in 19 apparently healthy individuals. In the cases of cholera and gastro-enteritis the tests were performed when dehydration was controlled and normal urination established. The results were as follows.

	Glomerular Filtration Rate (ml./minute)	Renal Plasma Flow (ml./minute)
Normal (19 individuals) ..	114±8	517±46
Cholera (14 patients)	60±12	272±46
Acute gastro-enteritis (6 patients)	41±16	193±64

Thus both the glomerular filtration rate and the renal plasma flow were greatly diminished in cholera and acute gastro-enteritis, and the authors suggest that this may be due to renal anoxia causing temporary diminution in blood flow through the cortex and not to any specific toxin of the disease. *C. L. Pasricha*

Allergy

866. **Localization of Blocking Antibody in Sera of Ragweed-sensitive Individuals by Starch Electrophoresis**
A. H. SEHON, H. Z. HOLLINGER, J. G. HARTER, A. E. SCHWEITZER, and B. ROSE. *Journal of Allergy* [*J. Allergy*] **28**, 229–237, May, 1957. 2 figs., 7 refs.

At McGill University Allergy Clinic, Montreal, the authors have attempted to locate the site of blocking antibody in the serum of ragweed-sensitive individuals by means of starch electrophoresis. Of samples of serum obtained from 6 patients sensitive to ragweed who had been given a course of ragweed pollen extract previously, 2 exhibited only weak blocking ability, but in the remaining 4 sera the blocking activity was found in the γ_2-globulin fraction and in one also in the γ_1-globulin fraction. *H. Herxheimer*

867. **Is Chronic Urticaria an Allergic Disorder?**
J. H. MITCHELL, D. L. SMITH, and R. A. MAYERS. *Annals of Allergy* [*Ann. Allergy*] **15**, 128–134, March–April, 1957. 15 refs.

The past history and present symptoms of 187 patients suffering from chronic urticaria were reviewed, with the object of determining whether there was reliable evidence for an allergic aetiology. It was found that skin reactions were positive in 6% only, and in 90% the differential eosinophil count was less than 5%. Focal infection did not seem to be frequent among these patients, but emotional disorders were frequently encountered. In 61% of cases the patient himself believed that emotional factors played a major part in the disorder. The authors contrast this picture with that of acute urticaria, where allergic aetiological factors can often be demonstrated. *H. Herxheimer*

868. **The Bronchodilator Effect of Compound 20025 (1-*o*-Chlorophenyl-2-*iso*propylaminoethanol Hydrochloride)**
R. E. JOHNSTON and R. E. SHIPLEY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 303–308, March, 1957. 3 figs., 4 refs.

A study of the effect of "Compound 20025" ("isoprophenamine") was made at the General Hospital, Indianapolis, Indiana, on 30 patients exhibiting evidence of bronchospasm. These patients were selected either because they were severe asthmatics or because they presented problems in management. In most cases the vital capacity and maximum expiratory flow rate were measured before and after varying oral doses of isoprophenamine ranging from 20 to 40 mg. per patient. Alleviation of bronchospasm and increase in vital capacity lasting for 2 to 8 hours were noted after administration of a single dose in some cases. To assess the long-term effects of the drug a number of patients were given doses varying from 20 to 40 mg. 4 times a day to 30 to 40 mg. 4-hourly for several months. The only side-effect of note was mild to moderate central nervous system stimulation. This was abolished when isoprophenamine was administered with an equal amount of amylobarbitone, which in such doses was not found to cause demonstrable sedation.

[Isoprophenamine, which is chemically related to isoprenaline, appears to be a potent, orally active bronchodilator agent. Moreover, it lacks the cardiac effects of isoprenaline and thus may be of great value in the treatment of bronchospasm associated with bronchial asthma.] *G. B. West*

869. **Use of Prednisone and Prednisolone in Treatment of Allergic Diseases**
E. B. BROWN and T. SEIDEMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 713–718, March 2, 1957. 1 fig., 8 refs.

Prednisone and prednisolone have been reported to be effective in various allergies, but no agreement seems to have been reached as regards dosage. The present authors therefore studied the optimum initial and maintenance dosage of these drugs in patients attending the Montefiore Hospital, New York, suffering from asthma, allergic rhinitis, and allergic dermatoses, the two drugs being administered interchangeably.

In 64 asthmatic patients an initial dosage of 10 mg. 4 times a day for 2 days was required, lower doses usually being inadequate. The dose was reduced within a week to 5 mg. 2 to 3 times a day. In 38 patients suffering from allergic skin disorders the drugs were most effective in self-limiting conditions such as acute contact dermatitis. Chronic contact dermatitis and atopic eczema also responded to treatment starting with 10 mg. 4 times a day and then reduced to a maintenance dose of 2·5 to 5 mg. a day or to 5 to 10 mg. every 7 to 10 days. Seasonal allergic rhinitis in 79 patients was far more effectively relieved by 15 to 20 mg. of the steroid drugs per day for 2 to 3 weeks than by antihistamine drugs. Perennial allergic rhinitis was promptly relieved in 9 patients by 10 mg. 4 times a day, with a maintenance dose of 5 mg. twice a day, but symptoms recurred within 2 to 6 weeks when treatment was stopped.

Side-reactions affected the central nervous system, leading to insomnia and euphoria; the gastro-intestinal system, leading to increase in appetite and abdominal discomfort of various types; and the genito-urinary system, leading to frequency of micturition. Other reactions included skin disorders, water retention, and glycosuria. Careful screening of patients for hypertension, pulmonary tuberculosis, diabetes mellitus, significant gastro-intestinal disease, and psychosis before treatment is started is advised.

The advantages of prednisone and prednisolone over cortisone and hydrocortisone are said to be the minimal dietary and salt restrictions necessary and the less frequent and less severe side-reactions. The authors stress that steroid therapy should be introduced only when safer methods have failed. *J. Pepys*

Nutrition and Metabolism

870. **Some Investigations on the Metabolism of Phenylalanine and Tyrosine in Children with Vitamin C Deficiency**
T. H. J. Huisman and J. H. P. Jonxis. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 77–81, April, 1957. 17 refs.

DL-phenylalanine and L-tyrosine were administered by mouth to three scorbutic children, and the excretion in the urine and the plasma levels of these and other amino-acids were determined. Both with and without additional tyrosine the excretion of tyrosine by scorbutic children was found to be much higher than by normal children. Since the plasma levels of phenylalanine and tyrosine were found to be low during the administration of these amino-acids, this amino-aciduria is thought likely to be of renal origin. As it has already been described by other authors the excretion of tyrosine substances is greatly increased in scorbutic children after the oral administration of tyrosine.—[From the authors' summary.]

871. **The Influence of Dietary Fats on Serum-lipid Levels in Man**
E. H. Ahrens, J. Hirsch, W. Insull, T. T. Tsaltas, R. Blomstrand, and M. L. Peterson. *Lancet* [*Lancet*] 1, 943–953, May 11, 1957. 12 figs., 30 refs.

Investigations are reported from the Rockefeller Institute, New York, on 40 patients with hypercholesterolaemia or hyperlipaemia, or with a normal blood cholesterol level but with definite signs of arteriosclerotic heart disease.

All the patients were free from renal, hepatic, or other complicating disease and were ambulatory. Most of the investigations were carried out in hospital in a metabolic ward, the patients receiving a liquid diet previously evolved and tested by the authors, the caloric content of which was adjusted so as to maintain a constant body weight. Protein contributed 15%, fat 40%, and carbohydrate 45% of the total calories, the protein being derived from milk and the nature of the fat being varied in different experiments. The diet was supplemented with vitamins, jodized salt, and ferrous gluconate. Most of the patients took this diet for a period of 4 to 6 months without interruption and without recognized ill effects, while one took it continuously for 36 months.

In one series of experiments the dietary fat in three successive periods was derived entirely from corn oil, coconut oil, and corn oil respectively, serum lipid levels being determined weekly for 8 weeks before the experiment and during each period. While not all patients responded to the corn-oil feeding in the same measure, the serum cholesterol and phospholipid levels generally fell sharply, usually within the first 2 weeks. In 16 cases they fell by 40% or more (the serum cholesterol level in one case falling from 1,089 to 175 mg. per 100 ml.) and in 22 others by at least 20%. In one case no statistically significant reduction of the serum cholesterol level could be achieved, and in another the reduction amounted to only 12%. On changing to coconut oil the levels of all serum lipids except the triglycerides rose again, and there was a further fall on reverting to corn oil, the mean serum levels of cholesterol and phospholipids in individual patients varying by no more than 10% from one corn-oil period to another. Addition of cholesterol to the corn-oil diet did not modify the reduction of the cholesterol level.

In 6 patients who subsequently took a totally vegetarian diet with supplements of 18 g. of β-sitosterol daily the serum lipid levels were in all cases very much higher than when the corn-oil formula was fed, indicating that the β-sitosterol content of corn oil was not responsible for its effect. In other experiments refined corn-oil was subjected to molecular distillation, the content of non-saponifiable material in the distillate being increased threefold and that in the residue being correspondingly reduced. Substitution of these two fractions in turn for the undistilled oil in the diet did not produce any change in the serum lipid levels during a test lasting 17 weeks, despite the sixfold difference in non-saponifiable content between the two fractions. Comparison of various fats showed that the effect on the serum lipid level was directly related to the degree of unsaturation of the constituent fatty acids as measured by the iodine value of the fat. If partially hydrogenated corn oil was used in the diet the serum lipid levels were proportionally higher. The substitution of natural fats and oils with a high content of fatty acids of short and intermediate chain length resulted in higher serum lipid levels than did that of fats containing long-chain saturated fatty acids.

The authors were unable to reach any definite conclusion as to whether the effect of dietary fat on serum cholesterol and phospholipid concentrations is more dependent on its mean unsaturation or on its content of a specific unsaturated acid—for example, linoleic acid. *Z. A. Leitner*

872. **Glucose Tolerance in Periodic Paralysis**
G. A. MacGregor and A. G. Shaper. *British Medical Journal* [*Brit. med. J.*] **1**, 917–921, April 20, 1957. 1 fig., 27 refs.

Investigations carried out at the Postgraduate Medical School of London on a patient with periodic paralysis, none of whose relatives were similarly affected, are described. The results of glucose tolerance tests and an intravenous insulin tolerance test indicated an abnormally increased tolerance of glucose, and it is suggested that the hypokalaemia and the paralysis in this condition are secondary effects of overactive glucose storage. *H. Harris*

Gastroenterology

873. **A Combined Cineradiographic and Manometric Study of the Gastro-oesophageal Junction**
G. S. M. Botha, R. Astley, and I. J. Carré. *Lancet* [*Lancet*] **1**, 659–662, March 30, 1957. 5 figs., 6 refs.

Muscular activity at the gastro-oesophageal junction was studied at the University of Birmingham in adult volunteers by slowly withdrawing from the stomach to the oesophagus a polythene tube attached to a capacitance electromanometer. The tube had an external diameter of 2·5 mm., and was passed through the nose after inducing local anaesthesia with a few drops of 4% lignocaine, which the subject was instructed not to swallow. Two types of tube were used, one of which had at its lower end a small balloon of thin latex (1 cm. long, with a capacity of 1 to 1·5 ml.), with radio-opaque markers to indicate its position, while the other had a hole at the end or at the side, the situation of which was similarly indicated by a radio-opaque marker. In all, 227 recordings were made from 18 normal subjects, 133 with the open tube and 94 with the balloon; in 129 cases simultaneous cineradiography was carried out with an image intensifier and an exposure of 0·01 second or less to avoid blurring. The subjects consisted of 11 medical students (8 men and 3 women) and 7 patients (6 men and 1 woman) in whom a radio-opaque clip had been attached to the anterior border of the oesophageal hiatus of the diaphragm at laparotomy at least 2 months previously, 6 having undergone partial gastrectomy for a peptic ulcer and one appendicectomy.

The " average " site at which the fall from intragastric to intra-oesophageal pressure occurred was the same with both types of tube; but the length of the segment over which the fall occurred was greater with the balloon tube, presumably owing to the length of the balloon. It was decided that the records made with the open tube were the more accurate ones, and therefore only the 133 such recordings, made on 14 of the subjects, are here analysed.

The form and situation of the pressure changes varied from subject to subject, and from time to time in the same subject. In 54% there was a preliminary rise in pressure before the fall to oesophageal pressure, and in 46% the pressure fell over a short segment with no such preliminary rise. In 11 of the 12 subjects in whom an intermediate zone of raised pressure was sometimes recorded the position of the gastro-oesophageal junction was located radiographically with barium, and in 6 cases the site at which the pressure began to rise was shown to be above this level. The site at which the pressure began to fall was above the level of the *x*-ray shadow of the dome of the diaphragm in 11 of the 14, the mean position for the whole group being 0·65 cm. above that level. The point at which the general intrathoracic pressure was reached was always above the diaphragm, the average distance being 2·15 cm. The total length of the segment over which these pressure changes were seen varied from 0·56 to 5·65 cm., with a mean of 2·6 cm. In 4 out of 6 subjects in whom the hiatus was marked with a clip the descent to general intrathoracic pressure began at a point above the clip, the mean distance for the group being 0·3 cm. Moreover, in the recordings in which there was a rise of pressure between stomach and oesophagus that rise was not constantly increased during inspiration. Hence it is concluded that the hiatus is not, or at any rate not solely, responsible for the increased pressure in the junction zone, and that there must also be an intrinsic sphincteric mechanism at the lower end of the oesophagus.

[It is unfortunate that the results are not tabulated in more orthodox statistical form so that the reader can draw his own conclusions from this wealth of experimental material.] *Denys Jennings*

874. **Radiological Localisation of the Diaphragmatic Hiatus**
G. S. M. Botha. *Lancet* [*Lancet*] **1**, 662–664, March 30, 1957. 4 figs., 8 refs.

The relative positions of the oesophageal hiatus and the dome of the diaphragm as seen on radiological examination were studied in 20 volunteers of average build (aged 27 to 63, 7 women and 13 men) in whom a metal clip was attached to the anterior hiatal margin immediately in front of the oesophagus at laparotomy. It is stated that " most of the patients " had undergone either partial gastrectomy or cholecystectomy, and only those were selected with benign lesions, normal anatomy, and good general condition. Within 2½ months careful *x*-ray studies were made. There was considerable variation from subject to subject, but in most cases the clip was well above the *x*-ray shadow of the dome of the diaphragm at the end of inspiration and well below the diaphragm at the end of expiration. During inspiration the clip moved downwards, inwards, and slightly backwards. The significance of these findings is discussed in relation to the assessment of disease in this region, particularly neoplasms, achalasia, diverticula, and hiatal hernia, and also in relation to observations on the nature of the gastro-oesophageal closing mechanism.

[The author states that " it has generally been accepted that the diaphragm, as seen in an antero-posterior radiograph, coincides with the level of the oesophageal hiatus ". Actually, the theory of *x*-ray image formation, as developed at the beginning of the century, was concerned with this very point, that the boundary between opaque abdominal contents and translucent lung was the part of the diaphragm tangential to the *x*-ray beam, and that this tangent did not necessarily bear any relation to the hiatus.] *Denys Jennings*

STOMACH AND DUODENUM

875. **Haemorrhages in Gastric Polyposis.** (Кровотечения при полипах желудка)
A. N. Protopopov. *Терапевтический Архив* [*Ter. Arkh.*] **29**, 37–41, No. 4, April, 1957. 2 figs., 25 refs.

The author reports the results of 205 clinical and radiological examinations carried out at the Saratov Medical Institute on patients with gastric polyposis, which in 65 cases was confirmed at operation or by gastric biopsy. Haemorrhage from the stomach occurred in 11 patients, in 4 of whom polypi prolapsed through the pylorus into the duodenum, in one the polyp became detached, and in 3 malignant change was observed. Complete or partial separation of polypi occurred in 6 cases, but in only one of these was there clinically recognizable gastric haemorrhage. Prolapse of polypi through the pylorus occurred in 12 further patients, resulting in 4 in massive gastro-intestinal bleeding. The majority of the patients presented a normal peripheral blood picture or only minor degrees of anaemia. Examination of the faeces for occult blood was conducted in 69 cases and gave a positive result in 31.

The author suggests that massive gastric haemorrhage is not typical of simple gastric polyposis, but that its occurrence indicates the presence of such complications as prolapse, separation, or malignant change. In particular the association of severe abdominal pain with massive intestinal haemorrhage is characteristic of separation, prolapse, or incarceration of the polypi.

Marcel Malden

876. **Gastroscopic Burns of the Gastric Mucosa**
N. M. Scott, J. A. Preston, and E. Palmer. *Gastroenterology* [*Gastroenterology*] **32**, 708–716, April, 1957. 5 figs., 2 refs.

Prompted by finding in a specimen obtained at gastric resection a lesion, suspected to be carcinomatous, which could have been a burn sustained during gastroscopy, the authors, at the Walter Reed Army Hospital, Washington, D.C., systematically studied the effect of gastroscopy on the gastric mucosa of dogs. Two clinical gastroscopes were used and the usual gastroscopic manipulations performed. The duration of gastroscopic examination was from 0·5 to 15 minutes, and animals were killed immediately after and at intervals of 3 days, one week, 2 weeks, and 4 weeks after the procedure.

The temperature of the tip of the gastroscope was found to reach 80° to 85° C. after a few minutes inspection of the mucosa. Burning was discovered even half a minute after introduction of the gastroscope. In general, the severity of the burn was increased in proportion to the duration of the examination. Visualization of such a burn was not easy because it was usually situated in the "blind" area of the posterior wall near the greater curvature. The characteristic appearance, as seen on subsequent gastroscopic examination, is a raised, dark red-brown surface, fading gradually to deep erythema at its edge and sharply demarcated from the gastric mucosa. Histologically, the lesion resembles an acute gastric ulcer. All burns healed without residual effects. The authors stress that gastroscopic burns may simulate a gastric ulcer or carcinoma, and that the possibility of their occurrence should be borne in mind in the clinical differential diagnosis of lesions of the posterior wall of the stomach. *I. McLean Baird*

877. **Antral Inhibition of Gastric Secretion**
P. H. Jordan and B. F. Sand. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **94**, 471–474, March, 1957. 1 fig., 6 refs.

This paper from the Veterans Administration Center and University of California Medical Center, Los Angeles, describes an experiment designed to demonstrate the inhibition of gastric secretion by free hydrochloric acid in the lumen of the pyloric antrum. In 4 dogs a Heidenhain fundal pouch was constructed; the pyloric antrum was isolated from the remainder of the stomach and duodenum and was divided to form two equal pouches, each of which was marsupialized. The duodenal stump was closed and a gastro-enterostomy performed. Experiments were started 3 weeks after operation.

Gastric secretion was stimulated in the fasting animal by perfusion of one antral pouch with 10% alcohol. When the response from the Heidenhain pouch was maximal the other antral pouch was perfused with hydrochloric acid (0·1 N). A significant decrease in acid production from the fundal pouch was observed to occur 1 to 3 hours later. It is suggested that this inhibition is mediated by a hormone released from the antral mucosa when in contact with free hydrochloric acid.

A. G. Parks

878. **Gastric and Duodenal Ulcer and Closed Craniocerebral Trauma.** (Язвенная болезнь желудка и двенадцатиперстной кишки и закрытая черепно-мозговая травма)
O. S. Radbil. *Терапевтический Архив* [*Ter. Arkh.*] **29**, 16–23, No. 4, April, 1957. 17 refs.

In an investigation of the connexion between closed head injury and peptic ulceration, carried out at the 1st Moscow Medical Institute, the author first analysed 2,000 case histories of patients with peptic ulcer and found that 11·6% of them had suffered a closed head injury in the past, in most cases during the war. Next he analysed 1,500 case histories of patients with various psychiatric disturbances; this revealed that 9·5% of them had peptic ulceration. Finally, 116 patients with peptic ulceration and a history of closed head injury were studied in detail; of these, 112 were men and 4 were women; they ranged in age from 20 to 40 years and 87 had duodenal and 29 gastric ulcer.

The investigation showed that in these patients the diseases tended to run an especially severe course, being accompanied by marked autonomic nervous disturbances, neurotrophic and neurovascular abnormalities, and a high incidence of intestinal haemorrhage, perforation, and marked disturbances of gastric motility. Test meals showed changes of gastric secretion resulting from dis-

turbances of cerebral cortical function. The author attributes this particularly severe course of peptic ulceration to the damaging effects of closed cerebral trauma on the normal balance between the processes of inhibition and stimulation within the cortical and subcortical centres of the brain, such imbalance resulting in disturbances of the vascular supply and motor and secretory function of the gastro-intestinal tract.

[These theoretical assumptions condition the author's detailed discussion of various prophylactic and therapeutic measures.] *Marcel Malden*

879. **A Case of Malignant Change in Two Peptic Ulcers, a Gastric and a Duodenal.** (Случай злокачественного перерождения язв желудка и двенадцатиперстной кишки)
I. Y. YUDIN. *Советская Медицина* [*Sovetsk. Med.*] 114–115, No. 1, Jan., 1957.

The case is described of a man of 58 who suffered from ulcer and carcinoma situated on the lesser curvature of the stomach which had given rise to massive metastases in the lymph nodes, liver, and omenta. Laparotomy was performed, but the patient died 3 days later from haematemesis and aspiration of vomited blood from a previously undiagnosed second ulcer situated in the duodenum. At necropsy histological examination showed that there was malignant change in this ulcer also. *A. Swan*

880. **Diseases Developing after Operations on the Stomach and Their Treatment.** (Болезни оперированного желудка и их лечение)
E. L. BEREZOV. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **35**, 24–32, No. 2, Feb., 1957.

When gastro-enterostomy was the operation of choice in the surgical treatment of peptic ulcer, about 30% of those subjected to the operation subsequently developed symptoms as severe, if not more so, as those of which they complained initially. Even after pyloro-antral resection complications arose, although the need for further surgery was much rarer. Such patients tended to seek medical rather than surgical advice, and the present author reviews 2,000 cases of dyspepsia following operation for peptic ulcer investigated and treated at Zheleznavodsk and Essentuki, spa stations in the Gorky district, between 1930 and 1940, representing 15 to 20% of all the patients seen during this period. A further series of patients operated on between 1951 and 1956 is also reviewed.

Medical treatment combined with spa therapy (diet, mineral waters, mud-baths, and general spa regime) was found adequate for most of the complications, which included gastritis, periduodenitis, pericholecystitis, and colitis. Further operative treatment, however, was necessary for the following conditions: (1) failure of the ulcer to heal (in 75% of cases); (2) recurrence of the ulcer or fresh ulceration (in 25 to 30% of cases); (3) development of a jejunal ulcer (in most cases); (4) gastro-colic fistula (in all cases).

During the period 1931–56 530 secondary operations were performed, the operative mortality being 9·6% up to 1948 and 5·5% between 1948 and 1951, while from 1952 to 1956 it was only 0·6% (one death out of 152 operations). Improved technique and the use of antibiotics were undoubtedly responsible for this improvement. Of the 152 cases treated during the period 1952–6, unhealed ulcers following gastro-enterostomy and operations for perforation accounted for 55; recurrent ulcer following the same measures, 11; "vicious circle", 7; jejunal ulcer, 25 (including 5 following gastrectomy); gastro-colic fistula, 13; cancer of the stomach, 19; cardiospasm, 2; and other complications, 20. Resection of the stomach was performed in 126 cases, including the 13 cases of gastro-colic fistula, transthoracic total gastrectomy in 9, and palliative operations (including restoration of normal anatomical relations and various types of anastomosis) in 17.

The author strongly recommends spa treatment, especially mud-baths, both before and after operation in cases of this type, as this will tend to reduce inflammation and adhesions and may in some cases even enable surgery to be dispensed with. It is emphasized that close liaison between physicians, radiologists, and surgeons is essential if the best results are to be obtained.
L. Firman-Edwards

881. **Comparisons of Gastric Emptying and Secretion in Men and Women, with Reference to Prevalence of Duodenal Ulcer in Each Sex**
M. BOOTH, J. N. HUNT, J. M. MILES, and F. A. MURRAY. *Lancet* [*Lancet*] **1**, 657–659, March 30, 1957. 2 figs., 8 refs.

A comparative study of gastric activity in healthy men and women was carried out at Guy's Hospital, London, in the hope of throwing light on the causes of duodenal ulcer, the incidence of which is markedly different in the two sexes. By means of a dye dilution method the volume of the gastric contents was estimated in 20 male and 19 female subjects 10 minutes after the administration through a stomach tube of 750 ml. of saline (100 mEq. NaCl per litre) at 37° C. and, in a second series of experiments, 20 minutes after the administration of 750 ml. of distilled water. Previous experiments had shown that a saline solution of this strength leaves the stomach at maximum speed, presumably because it has a minimal exciting effect on the duodeno-gastric inhibitory mechanism, whereas distilled water, which does excite inhibition, leaves the stomach at about half the rate of saline. Thus, the authors state, "by comparing the emptying-rates of equal volumes of saline and water an index of the activity of the duodenal brake may be obtained".

The mean estimated volume of saline leaving the stomach within 10 minutes was 357 ± 89 ml. in the men and 357 ± 131 ml. in the women, while the mean volume of distilled water leaving the stomach within 20 minutes was 423 ± 93 ml. in the men, and 406 ± 118 ml. in the women. [The standard differences given have been calculated from the standard errors of means quoted in the paper.] A scatter diagram is given, which "shows that those who empty saline solution quickly also empty water quickly". [No statistical measure of correlation

is given, however, and it is not easy to judge by eye how significant this is.]

The authors argue that as the saline solution leaves the stomach more rapidly than any other solution, it does not stimulate the "duodenal brake" at all, and that differences in the rate of emptying between subjects must therefore be due to differences in the propulsive power of the stomach. In view of the correlation demonstrated between the rate of emptying after distilled water and the rate of emptying after saline it is deduced that no important differences occur between subjects in the effectiveness of the duodenal inhibitory mechanisms, and that this is the same in both sexes. Hence, since there is no evidence of any sex difference in the propulsive power of the stomach or in its regulation by osmotic mechanisms, it is unlikely that these factors play any part in the pathogenesis of duodenal ulcer. The most likely explanation of the sex difference is that acid production on stimulation is greater in men than in women—about one and a half times higher in the present study. The alternative explanation that the duodenal mucosa is more vulnerable in men is discounted by the fact that a low level of gastric acid secretion after histamine is more commonly found among women with duodenal ulcer than among men with that condition. If the female duodenal mucosa was more resistant than the male to ulceration by acid the reverse would be the case.

[The objections to the authors' hypothesis are not discussed.] *Denys Jennings*

882. **The Controversial Relationship between. Blood Group A and Gastric Cancer**
I. HOGG and G. T. PACK. *Gastroenterology* [*Gastroenterology*] **32**, 797–806, May, 1957. 34 refs.

LIVER AND GALL-BLADDER

883. **Chlorpromazine Jaundice. Analysis of Twenty-two Cases**
J. L. WERTHER and B. I. KORELITZ. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 351–366, March, 1957. 4 figs., 46 refs.

Although jaundice as a side-effect of the administration of chlorpromazine has been known to occur since 1954, divergent opinions have been expressed concerning its clinical and pathological features and pathogenesis. The authors, working at the Mount Sinai Hospital, New York, have studied 22 cases of jaundice occurring after chlorpromazine administration over a period of 14 months and here present their findings.

Chlorpromazine jaundice is of a type unusual in relation to the administration of a drug. It is not a toxic hepatitis, as might be expected, but an obstructive jaundice due to intrahepatic biliary obstruction. The clinical features are typical of obstructive jaundice—acholic stools, biliuria, frequent pruritus, and fever. Tests of hepatic function give results quite characteristic of obstruction, and those reactions which would indicate parenchymal hepatic damage remain negative. In 6 of the authors' 22 cases liver biopsy was carried out, and photomicrographs are reproduced. In all specimens the liver parenchyma was normal or practically normal. The biliary system on the other hand always showed striking bile stasis, with plugs of inspissated bile in the canaliculi. In addition there was inflammatory reaction around the portal tracts, most of the inflammatory cells being eosinophil granulocytes. A mild eosinophilia was frequently noted in blood films from the jaundiced patients. The essential cause of the remarkable biliary obstruction remains undetermined; but, especially in view of the great eosinophil reaction around the portal tracts, an allergic reaction to the drug is postulated.

J. W. McNee

884. **Study of Chlorpromazine Jaundice, Its Mechanism and Prevention. Special Reference to Serum Alkaline Phosphatase and Glutamic Oxalacetic Transaminase**
H. SHAY and H. SIPLET. *Gastroenterology* [*Gastroenterology*] **32**, 571–591, April, 1957. 3 figs., 35 refs.

A study of 47 patients receiving chlorpromazine at the Temple University Medical Center, Philadelphia, showed that the level of serum alkaline phosphatase often rose before that of bilirubin in patients who were sensitive to the drug. In 11 patients a rise in serum alkaline-phosphatase level occurred after 5 to 18 days' administration of the drug. The authors suggest that serum alkaline-phosphatase determination twice weekly during the first 3 weeks of treatment with chlorpromazine would be a valuable screening procedure. If the level rises the drug should be withheld until a normal value is restored. The chlorpromazine may then be started again, and if there is no subsequent rise in alkaline-phosphatase level it may be assumed that desensitization has occurred and the drug may then be continued with impunity. Serum glutamic oxalacetic transaminase levels usually ran parallel to changes in alkaline-phosphatase values, but were thought to be less specific. *P. C. Reynell*

885. **Serum Transaminase in Liver Disease**
D. W. MOLANDER, E. SHEPPARD, and M. A. PAYNE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1461–1465, April 20, 1957. 7 figs., 3 refs.

The glutamic oxalacetic transaminase activity in the serum of patients with various hepatic syndromes was compared with the results of the usual tests of hepatic function, but no constant correlation was noted. The value for this enzyme in normal subjects has been shown to range from 5 to 45 units. In patients with Laennec's cirrhosis in whom there was evidence of progressive disease transaminase values were higher (range 28 to 286, mean 79 units) than in those whose disease appeared to be fairly static (range 13 to 150, mean 45 units). The values obtained in other liver diseases were: viral hepatitis, 540 to 1,890 units; biliary cirrhosis, 57 to 330 units; in obstructive jaundice (one case only) the value rose, but fell with relief of the obstruction; in one case of cinchophen intoxication the initial high enzyme value fell after cortisone therapy. The level of transaminase activity in the serum appears to be a sensitive

index of the degree of hepatic parenchymal necrosis, the level falling as the process of healing gets under way. It is stressed that in performing this procedure, since serially diluting the serum in the reaction mixture has the effect of increasing the transaminase titre, it is imperative to use the same volume of serum for any given patient when the test is being repeated.

W. H. Horner Andrews

886. **The Metabolism of Ammonia and α-Keto-acids in Liver Disease and Hepatic Coma**

W. H. J. SUMMERSKILL, S. J. WOLFE, and C. S. DAVIDSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **36**, 361–372, March, 1957. 6 figs., 35 refs.

The supposition that there is a causal relationship between ammonia intoxication and hepatic coma is supported by the demonstration of disordered ammonia metabolism in liver disease and of an increased ammonia level in the peripheral venous blood in hepatic coma, but these results might signify no more than impaired nitrogen metabolism secondary to liver disease.

At the Boston City Hospital (Harvard Medical School) 27 patients in impending hepatic coma or in coma, 16 males and 11 females between the ages of 29 and 70 years, were studied, together with 11 patients suffering from cirrhosis in the absence of hepatic coma and 18 patients without evidence of liver disease or renal or metabolic disorder. The diagnosis of liver disease was made on clinical and biochemical grounds, while histological confirmation was available in 27 patients, including 18 of the 20 patients who died in hepatic coma. In each group the ammonia concentration in both arterial and venous blood was determined.

In the control subjects and patients with uncomplicated liver disease the fasting levels of ammonia in arterial and venous blood were similar (up to 75 μg. per 100 ml.) and arterio-venous (A-V) differences showed a small and variable uptake or release of ammonia by the peripheral tissues. In impending coma the mean arterial ammonia level was 113 μg. per 100 ml., though one-quarter of the readings remained within the normal range, and the mean venous ammonia level was 92 μg. per 100 ml., one-half of the values remaining normal. There was a positive A-V difference in most cases. In comatose patients the mean arterial and venous ammonia concentrations were 193 and 139 μg. per 100 ml. respectively, with a smaller proportion of normal readings. The A-V difference was still predominantly positive, but relative equilibrium was not uncommon and tissue release of ammonia was sometimes observed. The arterial blood ammonia value in hepatic coma was related to the amount of nitrogenous material in the intestines and fell with protein withdrawal and with antibiotic treatment. The highest blood ammonia levels occurred in cases of coma precipitated by intestinal haemorrhage. Impairment of tissue uptake of ammonia was particularly striking in cases where the blood ammonia concentration was higher than 200 μg. per 100 ml. Elevation of the blood pyruvate and α-ketoglutarate concentrations occurred in parallel with that of the blood ammonia concentration in hepatic coma, while ammonium chloride administration led to a rise of the keto-acid levels in the blood in cases of liver disease generally, but not in control subjects. The authors assume that the increase observed in the level of keto-acids is caused by a defect in intermediate metabolism due to impaired utilization of ammonia and faulty removal of ammonia by the diseased liver. The concentration of pyruvate in the cerebrospinal fluid was comparable to that in the arterial blood, whereas the concentration of α-ketoglutarate, though above normal in hepatic coma, was comparatively small.

E. Forrai

887. **Relation of Hemorrhage from Varices to Mortality in Cirrhosis**

T. W. SHEEHY. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] **2**, 195–209, April, 1957. 2 figs., bibliography.

Exsanguination, hepatic failure, and infection are the three traditional causes of death in patients suffering from cirrhosis. In the series of 49 patients (aged 30 to 75 years) with Laennec's cirrhosis and bleeding oesophageal varices described in this paper from the Brooke Army Hospital, San Antonio, Texas, infection was inconsequential as a cause of death. Massive haemorrhage and shock caused the death of 10 patients despite treatment by tamponade, blood transfusions, and supportive therapy. Hepatic coma was even more lethal, and accounted for the death of a further 18 patients. Of a necropsy series of 102 cases of Laennec's cirrhosis studied at the same hospital during the same 5-year period (1950–4) haemorrhage was the cause of death in 48 cases. Clinically, as the author points out, even severe haemorrhage may be unsuspected, and clearly speed in treating haemorrhage is vitally important.

A. Wynn Williams

888. **The Mechanism of Sodium Retention in Cirrhosis of the Liver with Ascites: the Effect of Acetazolamide (" Diamox ") on Urinary Electrolytes**

R. HECKER. *Australasian Annals of Medicine* [*Aust. Ann Med.*] **6**, 75–82, Feb., 1957. 3 figs., 22 refs.

In this study, reported from the Postgraduate Medical School of London, acetazolamide, 250 mg. orally, was administered to 7 healthy control subjects, 5 cirrhotic patients without ascites, and 9 with rapidly accumulating ascites (7 with cirrhosis and 2 with extrahepatic portal hypertension). Initially the ascitic subjects showed lower urinary sodium:potassium ratios than did the non-ascitic patients. Acetazolamide tended to raise the ratio in the non-ascitic patients, but not in the ascitic patients, with the exception of one cirrhotic and one with extrahepatic portal hypertension. The urinary sodium output in the ascitic subjects before and after administration of acetazolamide was much lower than in the control subjects. The ascitic patients with low plasma sodium levels also showed low urinary sodium excretion, but when the plasma sodium concentration was normal the urinary sodium excretion varied widely, one patient with a high normal plasma sodium level consistently showing low urinary sodium levels. Bicarbonate excretion was much lower in the ascitic patients than in the other groups. This reduced diuretic effect of acetazolamide

in ascites is thought to be associated with urinary potassium rather than with urinary sodium excretion. It may be that the development of ascites in these patients is associated with excessive secretion of aldosterone, but the stimulus to the increased secretion of this substance is not known. *K. G. Lowe*

889. **Enlargement of the Parotid Gland in Disease of the Liver**
E. N. ROTHBELL and J. J. DUGGAN. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 367–372, March, 1957. 2 figs., 25 refs.

Six cases of non-inflammatory enlargement of the parotid glands in association with disease of the liver are described. The exact cause of this parotid enlargement is quite unknown, but the authors refer to a similar condition which may occur in malnutrition or starvation, in obesity, in diabetes mellitus, and in other nutritional disturbances. They infer that parotid enlargement in hepatic disease is simply to be taken as additional evidence of the important role which the liver plays in the nutrition of the body. *J. W. McNee*

890. **Motor Disorders of the Biliary Tract: a Clinical and Radiological Study.** (О нарушениях двигательной функции желчевыводящих путей по клинико-рентгенологическим данным)
A. G. TEREGULOV and K. A. MAYANSKAYA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **35**, 57–62, No. 2, Feb., 1957.

The normal motor function of the biliary ducts involves a complex mechanism. According to Odinov, Petrovskiĭ, Westphal, and other workers weak electrical stimuli applied to the vagus nerve produce contraction of the gall-bladder with simultaneous relaxation of the sphincter of Oddi, while stronger stimuli cause an increase in tone of the gall-bladder, an increase in bile concentration, spasm of the distal portions of the biliary tract (including the sphincter of Oddi), and retardation of the flow of bile into the duodenum. On the other hand stimulation of the sympathetic nerves causes a reduction in concentration of bile, hypotonus of the gall-bladder, and synchronous isolated spasm of the sphincter of Oddi.

The object of the study reported here was to elucidate the effects of disease of the gall-bladder and biliary tract on the motor function of the alimentary tract, and of alimentary disease on the motor function of the biliary system. The method employed was to perform simultaneous intravenous cholecystography with "bilitrast" and barium follow-through examination of the alimentary tract. A total of 173 cases were examined, 108 of biliary and 65 of gastro-intestinal disease. It was found that disease of the biliary tract generally caused a reduction in tone of the stomach, duodenum, and large bowel, with delayed evacuation. More rarely, increased tonus with accelerated peristalsis, sometimes accompanied by pylorospasm, was observed. In some cases the caecum was dilated and the distal colon spastic.

Of 12 cases of gastric and duodenal ulcer, contraction of the gall-bladder was accelerated in 7 and normal in 3, while in 2 the gall-bladder did not fill. Out of 53 cases of chronic appendicitis, in 12 the evacuation of the gall-bladder after a fatty meal was normal, in 36 it was delayed for 2½ to 3 hours, and in 5 it was accelerated. It appears, therefore, that there is a close relationship between the motor functions of the alimentary and of the biliary tracts, and that disturbance of the one may lead to marked disturbances of the other. This has to be reckoned with in radiological diagnosis, and the authors advocate this combined method of examination as being of great value, yet quite simple.
L. Firman-Edwards

INTESTINES

891. **Motility Patterns in the Terminal Ileum: Studies on Two Patients with Ulcerative Colitis and Ileac Stomas**
C. F. CODE, A. G. ROGERS, J. SCHLEGEL, N. C. HIGHTOWER, and J. A. BARGEN. *Gastroenterology* [*Gastroenterology*] **32**, 651–665, April, 1957. 4 figs., 19 refs.

This communication from the Mayo Clinic describes the results of motility studies of the terminal ileum in 2 male patients who had undergone ileostomy for ulcerative colitis. All measurements were made by balloon kymography, two balloons being passed through the stoma for a distance of 34 cm. from the stomal orifice, coming to rest about 3 cm. apart. Water was allowed to flow into the balloons under a pressure of 15 cm. H_2O and the motility patterns were recorded by photographic techniques; motility waves were classified according to their type and also the percentage of time each type of wave was present was calculated. The minimum control period of observation after an overnight fast was one hour. The effects of a meal and of the injection of 1 ml. of 0·9% sodium chloride solution subcutaneously, 0·5 mg. of neostigmine intramuscularly, $\frac{1}{100}$ grain (0·43 mg.) of atropine sulphate subcutaneously, and ¼ grain (16 mg.) of morphine sulphate were evaluated. A statistical comparison of motility patterns between the control and experimental periods was attempted.

Four main types of wave were noted. Type I was the basic rhythmic contraction, but changes in base-line pressure may also be non-rhythmic. Type-III waves were irregular Type-I waves superimposed on base-line pressure changes. The waves of Type IV were caused by simultaneous action of a number of adjacent sections of the ileum similar to the motor contractions of the colon; it is believed that waves of this type have not been previously described in the ileum. After the consumption of a hearty breakfast or after injection of neostigmine Type-I activity disappeared while Type-IV activity greatly increased. Atropine and other cholinergic blocking substances reduced all types of motor activity in the ileum. In contrast morphine reduced Type-IV waves but caused a decisive increase in waves of Type I and Type III.

The authors conclude that the Type-I waves observed in this study are significantly slower than the rate of basic rhythm in the upper ileum. [Waves of Type II are nowhere mentioned.] *I. McLean Baird*

Cardiovascular System

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The normal range, according to observations so far reported, varies from 0 to 11·2 mm. Hg. In 107 cases of hepatic cirrhosis observed by the authors at the Los Angeles County Hospital (University of Southern California School of Medicine) the average wedged hepatic venous pressure was 18·3 mm. Hg. In only one case in the whole series was it below 12 mm. Hg. The authors have found the estimation of wedged hepatic venous pressure useful in establishing a definite diagnosis of hepatic cirrhosis in difficult cases and, more important, in providing essential evidence in favour of, or against, the creation of a porta-caval shunt in patients who have had gastro-intestinal haemorrhage. The method can also be used to differentiate reliably between intrahepatic and extrahepatic portal obstruction in patients who are known to have oesophageal varices. *J. W. McNee*

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Aortic stenosis was accompanied constantly by a pressure gradient across the aortic valve during ventricular systole. The systemic blood flow was generally reduced and was a function of the pressure gradient and degree of aortic obstruction. The gradient alone was not an accurate measure of the degree of obstruction. In aortic stenosis, the pressure–volume elasticity relationships of the left ventricle are altered as a result of hypertrophy reflecting itself in elevation of the end-diastolic pressure. This did not correlate with clinical left ventricular failure. Total left ventricular work was one and one-half to two times normal. Giant " a " waves were characteristically observed in the left atrial pressure tracings.

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As might be expected, variations were found in both directions, but there were certain clear trends. After restoration of normal rhythm cardiac output increased, particularly after exercise; this was due to an increase

in stroke volume. Oxygen consumption was unchanged, but there was usually an increase in the oxygen content of pulmonary arterial blood with a corresponding reduction in the arterio-venous oxygen difference. Pulmonary arterial pressure was unchanged, but there was a tendency to an increase in pulmonary capillary pressure both at rest and during exercise. It was concluded that the circulation improves after the restoration of normal rhythm, but that the pulmonary capillary pressure may increase to an unfavourable degree. *C. Bruce Perry*

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CONGENITAL HEART DISEASE

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Pointing out that in view of the recent possibility of surgical correction of atrial septal defects their diagnosis and accurate location are now of paramount importance, the authors describe 5 cases (that is, about one-quarter of their small series of atrial septal defects) of ostium primum defect seen at the Medical College of Georgia, Augusta. In 4 cases the diagnosis was confirmed at operation, but no repair was attempted; in 2 of them there was an atrioventricularis communis with a functionally common atrium and in the other 2 associated mitral valve defect with incompetence. The diagnosis in the 5th case was made on the clinical findings only. The patients' ages ranged from 26 months to 34 years and all were female. Cardiac catheterization in the 4 cases operated on showed a left-to-right shunt at atrial level in all cases but in none at ventricular level, low arterial oxygen saturation in one, pulmonary hypertension in one, and pulmonary:systemic flow ratios varying from 1·6 to 4·1. In one case the catheter passed directly from the right atrium into the left ventricle but returned via the right ventricle, indicating the presence of an atrioventricularis communis.

It is pointed out that the features that differentiate an ostium primum lesion from the more common ostium secundum lesion are dependent on the associated abnormalities of the atrio-ventricular valves; they include clinical features of biventricular hypertrophy, mitral incompetence, and ventricular septal defect. A soft apical first sound is common, but has not so far been explained. An ostium primum defect with normal atrioventricular valves is rare and probably could be differentiated preoperatively from ostium secundum.

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Angiocardiographic studies in 60 cases of Fallot's tetralogy investigated at the Middlesex Hospital, London, are described. In all cases the aorta was found to be enlarged, with the two limbs more widely separated than usual, this latter finding being particularly marked in adults. A right-sided aortic arch was present in 12 of the cases, and in these cases the arch and its branches commonly formed a mirror image of the normal. An anomalous retro-oesophageal right subclavian artery was present in 6 (14%, compared with a frequency of 0·7% in the population as a whole). Examination of the pulmonary arteries revealed a markedly unequal division of the trunk in 19 cases; in 17 of these the left pulmonary artery was the larger branch, whereas normally the right branch is the larger. This inequality did not, however, appear to affect the filling of the two lungs.

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patients but clubbing of the fingers occurred in only one case. In all cases the electrocardiogram showed right ventricular hypertrophy. The haemoglobin value ranged from 14·0 to 18·0 g. per 100 ml.

Cardiac catheterization and gas analyses were carried out in each case, and the results are tabulated. The mean pulmonary arterial pressure varied from 7 to 17 mm. Hg, and the right ventricular systolic pressure from 70 to 138 mm. Hg. In all cases there was evidence of considerable pulmonary stenosis and left-to-right shunt, with a flow ranging from 1·3 to 6·9 litres per minute.

The combination seems to have a relatively good prognosis. While complete surgical correction is possible the risk appears to be excessive. The term " acyanotic tetralogy of Fallot " is put forward as a name for such cases. *David Friedberg*

899. **Association of Transposition of the Great Vessels and Rudimentary Right Ventricle, with and without Tricuspid Atresia**
A. KESSLER and P. ADAMS. *Pediatrics* [*Pediatrics*] **19**, 851–857, May, 1957. 2 figs., 7 refs.

CHRONIC VALVULAR DISEASE

900. **Transbronchial Pressure Measurement in the Left Auricle in the Diagnosis of Mitral Disease**
I. ANDERSEN, P. ESKILDSEN, M. JØRGENSEN, and T. POULSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **4**, 51–55, March, 1957. 10 figs., 6 refs.

This paper from the Copenhagen County Hospital reports a series of 108 cases in which the left auricular pressure was measured via the transbronchial route. Punctures were performed on 11 healthy control subjects, 57 patients with mitral disease subsequently verified by operation, 24 patients with heart disease upon whom no operation was performed, and 16 others in whom the procedure was a failure, only 3 of them being amongst the last 50. The method used was that introduced by Allison and Linden (*Circulation*, 1953, **7**, 669; *Abstracts of World Medicine*, 1954, **15**, 40), which was preferred to percutaneous transthoracic methods which may, in the authors' opinion, involve some difficulty and also some risk.

Transbronchial puncture is used as a routine in cases of mitral disease at this hospital, the puncture itself being painless and requiring no anaesthesia other than that used for bronchoscopy. The procedure takes only a few minutes, and no complications have been observed which could be attributed to the puncture, only one of the patients subsequently operated on showing slight staining of the pericardial fluid. The right main bronchus is pierced first, the needle usually entering the left atrium through the pulmonary artery, providing a recording of the pulmonary arterial pressure which the authors have found to be of great value in interpreting results. The apparatus used comprises a slender needle (internal bore 0·3 mm., length 6 cm.) attached to a 2-mm. bore metal tube 50 cm. in length which is connected to a condenser manometer through a 3-mm. bore polythene tube, the whole system being filled with heparinized saline. The puncture is made through an ordinary bronchoscope, the recording being made by means of a double-beam oscilloscope connected with an electrocardiograph, which permits direct reading and preliminary evaluation of the curve to be made during the puncture. [For technical details the original paper should be consulted.]

Punctures on the 11 normal subjects established the pattern of the normal curve and the normal left auricular pressure. A normal pressure curve, which has 3 waves, is reproduced together with a synchronously recorded electrocardiogram, and the waves and the manner of their causation are explained. From their own observations the authors find that the various mitral lesions apparently exhibit characteristic pressures and curves useful in preoperative diagnosis. In particular mitral insufficiency seems to be demonstrable with a fair degree of accuracy. In cases of pure stenosis and of pure or predominant mitral insufficiency interpretation of the curves is easy. Cases in which the two lesions are combined provide tracings which are more difficult to interpret, but which should be of diagnostic value. Examples of each type of curve are depicted and the diagnostic features enumerated. A record of the auricular pressure can also be useful in the follow-up of patients after operation. *L. G. Fallows*

901. **Hemodynamic Data during Rest and Exercise in Patients with Mitral Valve Disease in Relation to the Differentiation of Stenosis and Insufficiency from the Pulmonary Artery Wedge Pressure Pulse**
D. C. CONNOLLY and E. H. WOOD. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 526–544, April, 1957. 10 figs., 21 refs.

In this paper from the Mayo Clinic the authors present and discuss the haemodynamic findings in 24 patients with mitral stenosis and 20 patients with mitral insufficiency (as well as those in 3 cases of left ventricular failure not associated with mitral disease and in 16 healthy subjects) in an attempt to differentiate cases of mitral stenosis from those of mitral insufficiency. They point out that clinical, electrocardiographic, and radiological examinations are not always sufficiently accurate for this purpose so that occasionally fruitless thoracotomy and cardiotomy are performed on a patient whose sole or predominant lesion is mitral insufficiency.

No definite distinction between mitral stenosis and mitral insufficiency could be established by comparing the heart rate, cardiac index, pulmonary vascular resistance, and systemic arterial pressure in the two conditions, either during rest or during the response to exercise. When, however, the pulmonary arterial wedge pressure was correlated with the mean peak of the systolic (V) wave a significant relationship was observed and a distinct separation between cases of mitral stenosis and mitral insufficiency became evident. Thus when the pulmonary artery wedge mean pressure exceeded 20 mm. Hg, the peak V-wave pressure was significantly greater in mitral insufficiency than in mitral stenosis at equivalent

levels of pulmonary arterial wedge pressure, and there was no overlap between the groups. No such distinction was observed between the two groups, however, when the mean pulmonary arterial wedge pressure was less than 20 mm. Hg, unless this pressure could be increased above 25 mm. Hg by exercise.

The prominence of the V wave in mitral insufficiency is caused by the regurgitation of blood into the left atrium during ventricular systole, the pulmonary arterial wedge pressure pulse being a moderately damped, but reasonably accurate, representation of the left atrial pulse in pressure and usually in contour. Criteria are given for deciding if the tip of the catheter is accurately wedged, and other methods for differentiating the two types of mitral disease are considered. Other haemodynamic findings not found to be of use in differentiating such cases are: (1) the time interval from the Q wave in the electrocardiogram to the peak of the V wave; (2) the time of onset of the V wave in relation to the Q–T interval; and (3) the pulmonary arterial diastolic pressure considered in relation to the pulmonary arterial wedge mean pressure. In one of the present cases a misleading deduction was made from analysis of the pulmonary arterial wedge pulse and the presence of a considerable gradient across the mitral valve; operation showed, however, that the patient had severe mitral stenosis but no insufficiency. *H. E. D. Lloyd*

902. **Surgical Treatment of Aortic Stenosis**
R. Brock. *British Medical Journal* [*Brit. med. J.*] 1, 1019–1028, May 4, 1957. 9 figs., 27 refs.

The author discusses the clinical features and surgical treatments of aortic stenosis with reference to the results of 120 operations carried out in such cases. The development of surgery of the aortic valve is considered and the part that can be played by valvotomy indicated. Though conservative treatment is still often urged on the grounds that the expectation of life may be long, it is pointed out that this is only occasionally the case and that the condition may occur in comparatively young people. Out of 78 patients with severe symptoms, 31 were below 40 and 56 below 50 years old.

Assessment of the patient's clinical state should not depend on symptoms—the left ventricle is capable of a considerable degree of compensation and the presence of obvious symptoms may indicate the onset of failure. More exact measurement of the load on the heart must be obtained. The figures and curves obtained from comparison of the pressures in the left ventricle, measured by direct percutaneous puncture, and brachial artery give an actual picture of the pressure gradient across the stenosed valve, which is usually in the region of 50 mm. Hg, though it may reach double this figure. This should be confirmed at operation by direct puncture of the left ventricle and aorta. Apart from fusion of the valve cusps in aortic stenosis there is a considerable degree of distortion, and calcification is frequent. The rock-like valves that are sometimes encountered cannot be mobilized except at the risk of severe incompetence, and it is doubtful whether " cure " is ever possible when the valves are calcified. Calcification is less common in aortic stenosis associated with mitral valvular disease, 20 out of 34 such cases in the author's series being free from this complication.

The operation favoured by the author is a transventricular " blind " valvotomy, though 6 operations have been performed with an " open " transaortic technique under hypothermia. A left antero-lateral thoracotomy through the bed of the 5th or 6th rib is used. The carotid arteries are isolated and encircled by check ligatures, which are tightened if there is any risk of an embolus of calcium being dislodged during operation. [The author's description of his technique should be read in the original.] Ventricular fibrillation may occur as a result of the intracardiac manipulation and should be treated actively as soon as an effective valvotomy has been achieved. If aortic stenosis exists with mitral stenosis the mitral lesion is treated first. The obstruction to the ventricular inflow will have protected the left ventricle to some extent and renders the aortic valvotomy more straightforward.

Combined mitral and aortic valvotomy was undertaken in 34 of the author's cases, with 3 operative deaths (due to the mitral lesion). In 12 cases the result was " good " or " excellent ". Four patients have since died. There were 2 cases of aortic stenosis associated with coarctation, both lesions being severe.

Excluding 5 cases of subvalvular stenosis and one in which valvotomy was not carried out there were 78 cases of isolated aortic stenosis, some of which, particularly the early cases, were very bad risks. The over-all mortality was 18%, but excluding the first 8 cases it was 12·8%, and of the last 48 patients treated, only 3 have died. Of the 64 survivors, 9 have since died; the results in 42 can be classed as " good " or " excellent ". Regurgitation following operation was observed in 14 cases and in 4 cases was responsible for later death, but in some cases preoperative regurgitation has been relieved.

The author concludes with a critical appraisal of the methods for treating aortic stenosis and is clearly in favour of the transventricular approach if any calcification of the valve is suspected. *T. Holmes Sellors*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

903. **Prognosis of Coronary Heart Disease in Medical Practitioners**
J. N. Morris, J. A. Heady, and R. G. Barley. *British Heart Journal* [*Brit. Heart J.*] **19**, 227–232, April, 1957. 2 figs., 18 refs.

This study by the Social Medicine Research Unit of the Medical Research Unit of data provided by the records of a large medical assurance society is an extension of one previously reported by the same authors (*Brit. med. J.*, 1952, **1**, 503; *Abstracts of World Medicine*, 1952, **12**, 183). All male medical practitioners aged 40 to 64 holding a sickness insurance with the society who suffered a first clinical attack of coronary heart disease between January 1, 1940, and December 31, 1952, have been followed up to December 31, 1954. There was a

total of 316 such attacks: in 252 of these the final diagnosis of the first attack was coronary occlusion, coronary thrombosis, or myocardial infarction, in 52 the diagnosis was angina pectoris or angina of effort, and in 12 the diagnosis was coronary insufficiency. Of the 316 patients, 24% died in the first week and 29% in the first month, whereas 68% survived to the end of the first year and 54% to the end of the fifth year after the first attack. The majority of the early deaths occurred among patients with a diagnosis of coronary occlusion. All those with a diagnosis of angina pectoris or angina of effort survived to the end of the first month, only 2% dying before the end of the first year, whereas 30% of those with coronary occlusion died in the first week. That the danger is greatest in the first week is shown by the fact that of those who survived this period, 70% survived another 5 years and 50% 10 years. At all times the prognosis was slightly better in the younger age groups. *C. Bruce Perry*

904. **Thyrotoxicosis and Myocardial Infarction.** [In English]
G. GRYTTING and H. A. SALVESEN. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 169–171, April 18, 1957. 6 refs.

Only one case of coronary infarction has been found among 426 women and 95 men over the age of 40 with thyrotoxicosis seen at Rikshospitalet, Oslo, during the last 20 years. This was in a woman of 46 who had in any case suffered from angina pectoris for 2½ years before the thyrotoxicosis developed. This low incidence accords with what might be expected having regard to the causal relationship between hypercholesterolaemia and myocardial infarction, the blood cholesterol level being characteristically subnormal in thyrotoxicosis. The average serum cholesterol level in 378 cases in the present series was 160 mg. per 100 ml., which is significantly lower than the normal for the age group. Necropsy on the 15 patients who died showed the occurrence of atheroma to be minimal—coronary atheroma being present in 5 and aortic atheroma in 11—and inversely related to the duration of the thyrotoxicosis.

The authors, while aware that their survey has little statistical value, nevertheless suggest that it " does not contradict the supposition that a thyrotoxic state may afford a certain protection against coronary sclerosis ". *Gerald Sandler*

905. **The Origin and Course of Myocardial Infarction.** (Происхождение и течение инфаркта миокарда)
P. E. LUKOMSKIĬ and E. M. TAREEV. *Советская Медицина* [*Sovetsk. Med.*] 3–33, No. 1, Jan., 1957. 11 figs.

The authors present the findings of a detailed study of 1,099 cases of myocardial infarction, together with some observations on an additional group of 500 cases. The age incidence showed a peak (41·2% of the cases) in the 6th decade of life. Men and women were affected in the ratio of 2·2 to 1, but this sex difference tended to diminish with age. Almost 42% of all patients suffered from hypertension. Atherosclerosis of the coronary arteries was found in 96·8% of 185 cases examined post mortem, and coronary thrombosis in 58·6%. A history of attacks of anginal pain preceding the infarction by months or years was obtained in 83% of 997 patients; thus only 17% of the patients were free from such attacks. The blood cholesterol level was not in general markedly raised, exceeding 250 mg. per 100 ml. in only 9·3% of cases. Pain was a prominent symptom in 95·6%. It was precordial in 69·6% of cases and retrosternal in 26·2%; radiation of the pain to sites other than the left arm and shoulder was observed in only 5%. Occasionally the character of the pain did not differ from that of a simple angina, and for this reason the infarction was missed clinically in several cases. Pain of short duration (less than one hour) was found to be associated with lower mortality. Pyrexia, usually not exceeding 38° C. (100·4° F.), was present in 69% of patients. The rise in temperature occurred as a rule within the first 3 days of the attack and usually subsided during the next 2 weeks, although in 9% of cases it persisted for up to 6 months, simulating a chronic infection. There was no relation between the increase or duration of temperature and mortality. Leucocytosis, on the other hand, appeared to have prognostic significance, the mortality among patients with a leucocyte count exceeding 15,000 per c.mm. being more than double that among those with a lower count. The erythrocyte sedimentation rate was raised in 89% of cases, varying from 11 to 60 mm. per hour; in about half the cases the initial rise was observed during the first 3 days.

Mortality after a second infarction was found to be about 46% higher than after the first, and was much higher in cases with severe shock, cardiac insufficiency, and cardiac arrhythmia than in cases not thus uncomplicated. Hypertension was also shown to influence the mortality unfavourably, as also did the patient's age. Rupture of the heart was discovered at necropsy in 24 out of 179 cases " of atherosclerotic nature ". In the majority of these cases this occurred during the first week, the incidence showing a decline from the third day of the illness. Anterior infarcts constituted 41·9% of the total, and posterior infarcts 30·1%. Additional involvement of the interventricular septum raised the mortality from an average of 8·3% to 19·1%. The greatest number of deaths occurred during the first 24 hours after admission to hospital. Treatment along the usual lines is discussed. *A. Swan*

906. **The Fatty Acids of the Blood in Coronary-artery Disease**
A. T. JAMES, J. E. LOVELOCK, J. WEBB, and W. R. TROTTER. *Lancet* [*Lancet*] **1**, 705–708, April 6, 1957. 1 fig., 13 refs.

Gas–liquid chromatography was used to determine the proportions of a range of fatty acids, from C_6 to C_{20}, in the blood of twelve patients with coronary-artery disease and in twelve controls matched for sex and age. For the purpose of this analysis the blood was divided into red-cell, plasma-phospholipid, and plasma acetone-soluble fractions.

In the red-cell and plasma-phospholipid fractions there were no detectable differences between the proportions of any fatty acids in the patients and their controls.

In all three fractions the mean proportions of the "essential fatty acids" (linoleic and arachidonic) were about the same in the patients and in the controls. Hence these observations do not support the hypothesis that deficiency of these "essential fatty acids" is a factor in the genesis of coronary-artery disease.

In the acetone-soluble fraction of the plasma (containing cholesterol esters and glycerides) there was some suggestion of an increase in the combined proportions of mono-unsaturated C_{14}, C_{16}, and C_{18} acids in the patients compared with the controls. The ratio of the most abundant of these acids (oleic) to its corresponding saturated acid (stearic) was higher in the patients with coronary-artery disease. The implications of this observation cannot be properly assessed without further resolution of the acetone-soluble fraction into its two components, cholesterol esters and glycerides.—[Authors' summary.]

907. **The Treatment of Patients Suffering from Angina Pectoris by Means of a Ganglion-blocking Agent—"Gangleron".** (Лечение больных грудной жабой ганглиоблокирующим препаратом—ганглероном)
N. M. Davidovskiĭ. *Терапевтический Архив* [*Ter. Arkh.*] **29**, 51–58, No. 4, April, 1957. 1 fig., 4 refs.

"Gangleron", a ganglion-blocking agent recently developed in the Soviet Union, is chemically a hydrochlor-diethylaminoalkyl ester of para*iso*butyloxybenzoic acid. It blocks the N-cholinergic receptors in parasympathetic ganglia but not the M-cholinergic receptors, and it also weakens the transmission through the sympathetic synapses. It is said to be of low toxicity. Holding that the occurrence of angina pectoris is due to spasm of the coronary arteries arising from central disturbances of their innervation, the author decided to try this drug in the treatment of coronary insufficiency in 80 patients with angina, 62 men and 18 women, investigated at the 1st Leningrad Medical Institute, of whom 41 patients were suffering from hypertension, 34 from myocardial infarction, and 5 from coronary angioneurosis.

Gangleron was administered subcutaneously in doses of 2 or 3 ml. of a 1·5% solution 3 or 4 times a day. After about 10 days similar doses were administered orally. In a proportion of cases gangleron was also given by intracutaneous injection (20 to 30 ml. of a 0·25% solution) into the areas of hyperalgesia or referred pain. The duration of in-patient treatment varied from 2 to 4 weeks. The results as judged by diminution in the duration, frequency, and severity of anginal attacks, were "excellent" or "good" in 65% of cases, while 31·2% were improved and no effect was noted in 3·8%. Beneficial effects were least marked in patients with hypertension and a history of myocardial infarction. In the dosage employed gangleron had only a minimal purely hypotensive effect. Serial electrocardiographic studies suggested that the therapy resulted in an actual improvement in the coronary blood flow. There were no untoward side-effects and no manifestations of chronic toxicity. The long-term follow-up of 52 of the patients showed that although the benefit from a single course of gangleron therapy persisted for an appreciable time, the patients who were discharged on maintenance treatment (12 out of 52) fared much better than those not so treated and were all able to return to their previous occupations.

The author suggests that gangleron is an effective agent for the treatment of angina pectoris and that it is best given in the form of continuous therapy.

Marcel Malden

908. **Retrosternal Procaine Anaesthesia in the Treatment of Patients with Coronary Insufficiency.** (Загрудинная новокаиновая анестезия в лечении больных с коронарной недостаточностью)
F. E. Ostapyk. *Терапевтический Архив* [*Ter. Arkh.*] **29**, 58–70, No. 4, April, 1957. 7 figs., 13 refs.

The sensation of anginal pain depends on the transmission of pain impulses along the nerve plexuses in the anterior mediastinum. The left plexus, lying as it does in front of the aortic arch and behind the manubrium sterni, is particularly accessible to procaine infiltration. The injection, consisting of 60 to 80 ml. of a 0·5% solution of procaine warmed to 36° to 37° C., is given through a long (15- to 18-cm.) needle introduced through the suprasternal notch along the posterior wall of the manubrium.

At the Central Institute of Postgraduate Medical Education, Moscow, the author gave 320 such injections to 55 patients suffering from coronary insufficiency, 56 of them being administered during an attack of pain and 9 during a recurrence of myocardial infarction. The series included 27 patients with coronary arteriosclerosis, 24 with hypertension, and one case each of rheumatic heart disease, thyrotoxicosis, generalized neurosis with cardiac pains, and painless coronary insufficiency. The injections were repeated more than once in a majority of the patients at intervals varying from one day to one week. A single injection of procaine stopped anginal pain or an attack of cardiac asthma immediately in almost all cases, although some had not previously responded to injections of morphine, atropine, or application of leeches to the praecordium. The beneficial effects of a single injection lasted on the average from 10 to 48 hours. Serial electrocardiograms showed improvement in coronary circulation. After a course of injections a majority of patients remained free from pain [for an unspecified period of time].

Toxic symptoms, consisting mainly in feelings of dizziness and generalized weakness, occurred transiently in most of the patients, but were troublesome only in 5. In 2 cases, however, these symptoms were associated with a worsening of the coronary pain, this being attributed to the fall in blood pressure which takes place after the injections. On 8 occasions a major blood vessel was entered—the left innominate vein 6 times and the aorta twice—but no permanent damage ensued.

In the author's opinion retrosternal procaine anaesthesia offers an effective means of treating coronary insufficiency, although he agrees that the treatment does not in any way affect its basic cause. *Marcel Malden*

BLOOD VESSELS

909. **Surgical Treatment of Coarctation of Aorta**
W. R. RUMEL, C. P. BAILEY, P. C. SAMSON, and D. H. WATERMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **164**, 5–7, May 4, 1957. 5 refs.

A study of 1,601 cases of coarctation of the aorta treated surgically by 36 members of the surgical advisory committee of the American College of Chest Physicians indicates that the over-all operative mortality rate was 8·6%. A satisfactory clinical result was obtained in 96·3% of the survivors. The most frequent causes of death and their respective incidences were as follows: (1) various cardiovascular complications, 37·7%; (2) disruption of the anastomosis, 20·7%; and (3) hemorrhage at the time of surgery, 11·8%.

The results obtained to date are good enough to justify general application of the surgical treatment of coarctation of the aorta. In the future, better results undoubtedly will be obtained by: (1) operation before patients enter the advanced age group; (2) operation earlier in infants and young children; (3) more adequate management of serious associated defects; and (4) improvement, as a result of further experience, of management of the technical problems peculiar to the condition.—[Authors' summary.]

910. **Aortic Aneurysm. Report of 101 Cases**
B. ROBERTS, G. DANIELSON, and W. S. BLAKEMORE. *Circulation* [*Circulation (N.Y.)*] **15**, 483–491, April, 1957. 40 refs.

911. **Clinical Evaluation of Three Anticoagulants in Thromboembolic Disease**
J. McE. NEILSON and A. W. MOLLISON. *British Medical Journal* [*Brit. med. J.*] **1**, 1214–1217, May 25, 1957.

The results obtained with three anticoagulants in the treatment of thromboembolic disorders have been compared at Stobhill General Hospital, Glasgow: 57 patients received cyclocoumarol (" cumopyran "), 125 ethyl biscoumacetate (" tromexan "), and 179 phenindione (" dindevan "). It was noted that prolongation of the prothrombin time to a therapeutic degree—namely, 2 to 3 times the control value—was effected more quickly with dindevan and tromexan than with cumopyran. When a steady maintenance dose was given, fluctuation of the prothrombin time was less marked with dindevan than with the other two anticoagulants. Haemorrhagic manifestations during therapy occurred in 8·7% of cases treated with cumopyran, 6·1% with dindevan, and 4·8% with tromexan.

The response to administration of vitamin K_1 was similar, though repeated doses were required when the long-acting drug cumopyran was given. It is considered that dindevan is a more satisfactory and more easily controlled anticoagulant than either tromexan or cumopyran. *A. G. Freeman*

912. **Mechanical Factors in Atherosclerosis**
J. B. DUGUID and W. B. ROBERTSON. *Lancet* [*Lancet*] **1**, 1205–1209, June 15, 1957. 1 fig., 23 refs.

SYSTEMIC CIRCULATORY DISORDERS

913. **Methoxamine: Effect on Blood Pressure and Renal Hemodynamics**
L. C. MILLS and J. H. MOYER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 409–417, April, 1957. 3 figs., 11 refs.

The changes in blood pressure, glomerular filtration rate, and renal plasma flow in 7 normotensive subjects following the intravenous infusion of a sympathomimetic amine, methoxamine (" vasoxyl "; β-hydroxy-β-(2:5-dimethoxyphenyl)-*iso*propylamine hydrochloride), were studied at the Jefferson Davis Hospital (Baylor University College of Medicine), Houston, Texas. The average dose was 13·9 μg. per kg. body weight per minute, and renal clearance was measured over 2 to 4 consecutive 10-minute periods when the desired blood-pressure response had been obtained.

The average increase in mean blood pressure (diastolic pressure + ⅓ pulse pressure) was 36%, systolic pressure increasing more than diastolic, and was associated with a vagal bradycardia (annulled by atropine). The glomerular filtration rate and renal plasma flow fell significantly in most cases, the average values being 63% and 67% respectively of the control values, and the total renal vascular resistance increased in all cases. Urine flow decreased, sodium excretion increased, and the effect on potassium excretion was variable. Side-effects included pilomotor responses in all cases and spasm of the bladder in some.

The renal effects of methoxamine are compared with those of noradrenaline, as reported by Mills *et al.* (*Clin. Res. Proc.*, 1956, **4**, 41), and of " aramine " (" metaraminol "), as described by Livesay *et al.* (*Amer. Heart J.*, 1954, **47**, 745; *Abstracts of World Medicine*, 1954, **16**, 446). For a similar rise of blood pressure aramine produced no decrease in glomerular filtration rate or renal plasma flow, noradrenaline caused a significant depression of renal plasma flow, and methoxamine reduced both glomerular filtration rate and renal plasma flow. To explain these results the authors suggest either increased sensitivity of the renal vascular adrenergic receptors to methoxamine, or a differential effect of the drugs on cardiac output with a consequent varying degree of vasoconstriction to produce the same rise in blood pressure. The risk of renal depression in this treatment is pointed out. *Gerald Sandler*

914. **Vasomotor Responses in the Extremities of Subjects with Various Neurologic Lesions. I. Reflex Responses to Warming**
W. REDISCH, F. T. TANGCO, L. WERTHEIMER, A. J. LEWIS, and J. M. STEELE. *Circulation* [*Circulation (N.Y.)*] **15**, 518–524, April, 1957. 3 figs., 38 refs.

This paper reports work which has been carried out at the Goldwater Memorial Hospital (New York University College of Medicine), New York, in order to elucidate the behaviour of the blood vessels in sympathectomized limbs, the vascular responses in such limbs to distant body warming being compared with those in the limbs of normal subjects, both young and

old, of elderly patients with obliterative arterial disease and of hemiplegic and paraplegic patients. Plethysmographic recordings from the foot and leg and skin temperature readings were made in groups of subjects in the above categories in controlled environmental conditions, the groups consisting of 4 to 12 subjects each.

In the hemiplegics the paralysed and non-paralysed legs responded to distant body warming with an increase in blood flow and rise in skin temperature comparable to those seen in normal subjects; the basal flow in paralysed legs was higher than that in their fellow normal limbs. The 4 patients with transection of the spinal cord on the other hand varied in their behaviour, both increase and decrease in flow being noted. Sympathectomized legs tended to respond to distant warming with a reduction in blood flow; the raised skin temperature in such limbs did not fall as the total flow decreased.

It is pointed out that the cerebral lesions in the hemiplegics evidently did not affect the vasomotor responses in the legs, whereas some of the spinal lesions did; the extent of the spinal lesions was not exactly known in all cases, though the legs of all hemiplegic patients were anhidrotic. It is suggested that the reduced flow in sympathectomized limbs following distant warming is not due simply to deviation of blood elsewhere, but also to the liberation of adrenaline by the warming process, preliminary observations having indicated that adrenergic blockade diminishes the abnormal constrictor response.

C. J. Longland

PULMONARY CIRCULATION

915. **Respiratory Factors Affecting Pulmonary Arterial Blood Pressure and Flow through the Lungs**

D. F. Heiman, S. Rodbard, A. B. Shaffer, and G. L. Snider. *Journal of Applied Physiology* [*J. appl. Physiol.*] 10, 31–36, 1957. 5 figs., 15 refs.

Recorded pulmonary arterial pressure is the sum of the intraluminal pulmonary blood pressure and the surrounding intrathoracic pressure. It usually rises in inspiration and falls in expiration, these fluctuations being marked in some heart diseases. Records of pulmonary arterial pressure, ventilatory data, and intraoesophageal pressure in 5 cases undergoing cardiac catheterization at the Michael Reese Hospital, Chicago, were analysed in an attempt to determine whether the pressure changes were due to true intraluminal blood-pressure changes or to variations in intrathoracic pressure. Pulmonary arterial pressure was recorded with a cardiac catheter. True intraluminal pressure was derived from this by deducting the intrathoracic pressure recorded by means of a balloon in the oesophagus.

In one case a satisfactory estimate of respiratory variations could not be made because of marked cardiac irregularity. In 2 cases of mitral stenosis with tricuspid insufficiency both the recorded and the intraluminal end-diastolic pulmonary arterial pressures fell during inspiration and rose during expiration. In one case of mitral stenosis and one of lung sarcoidosis the recorded blood-pressure changes were as above, but the intraluminal pressure rose in inspiration and fell in expiration.

Because of increased venous return the intraluminal pulmonary arterial pressure might be expected to rise in inspiration. Its failure to do so in the 2 cases of tricuspid insufficiency might be due to a fall in right ventricular stroke volume as a result of regurgitation. Another factor causing intraluminal pressure to rise during inspiration might be increased pulmonary vascular resistance. Evidence of this was found in one case of mitral stenosis during voluntary hyperpnoea. Intraluminal pressure rose at the end of diastole, which lasted throughout most of inspiration. Towards the end of diastole, pulmonary flow would be decreasing. Increased pressure independent of respiratory changes must therefore be due to increased resistance.

D. Goldman

916. **Pulmonary Arterial Pressure after Priscoline in Mitral Stenosis**

K. Braun, G. Izak, and S. Z. Rosenberg. *British Heart Journal* [*Brit. Heart J.*] 19, 217–221, April, 1957. 1 fig., 27 refs.

At the Rothschild–Hadassah University Hospital, Jerusalem, 14 patients with predominant mitral stenosis, confirmed at operation, were studied. After pulmonary and brachial arterial pressures had been measured by electromanometer 25 mg. of " priscoline " (benzazoline) was injected into the pulmonary artery through the catheter. Cardiac output (Fick principle) was determined before and again 10 and 30 minutes after the injection. A significant fall in the pulmonary arterial pressure was observed and a slight fall in brachial arterial pressure. The changes observed in the calculated cardiac output were judged to be unreliable.

It is concluded that benzazoline diminishes pulmonary vascular resistance in mitral stenosis by virtue of its sympathicolytic and adrenolytic effects.

H. E. Holling

917. **Influence of Acetylcholine on the Pulmonary Arterial Pressure**

P. Harris. *British Heart Journal* [*Brit. Heart J.*] 19, 272–278, April, 1957. 3 figs., 25 refs.

It is still uncertain whether active variation in the calibre of the vessels of the pulmonary circulation can be produced by pharmacological stimuli, and reports of the action of acetylcholine have so far been conflicting. At King's College Hospital, London, the author has therefore investigated the effect of this substance in 47 patients with various cardiac abnormalities causing different degrees of pulmonary hypertension. Doses of acetylcholine varying from 0·25 to 8·0 mg. were injected into the pulmonary artery. A transient fall of pulmonary arterial pressure was caused by acetylcholine in 18 of the 47 patients, this fall being most marked in patients with a moderately raised pressure; no change occurred when the pulmonary arterial pressure was normal or greatly raised. It is suggested that the results may be related to structural alterations occurring in the small pulmonary arteries in association with pulmonary hypertension.

H. E. Holling

Haematology

918. Radioactive Vitamin B_{12} Studies. Experience with the Urinary Excretion Test and the Measurement of Absorbed Plasma Radioactivity

S. R. GOLDBERG, B. K. TRIVEDI, and L. OLINER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 583–589, April, 1957. 1 fig., 8 refs.

At the Michael Reese Hospital, Chicago, the authors have studied both the urinary excretion and the plasma levels of vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt (^{60}Co) after the oral administration of a test dose. They confirm the finding of other workers that the levels of vitamin-B_{12} excretion in Addisonian pernicious anaemia are always lower than in other conditions, with the exception of certain cases of kidney disease, or in normal subjects. Measurement of the plasma level of radioactivity was found to afford a reliable measure of absorption of a test dose of the vitamin if 1 μc. or more was given, the peak of activity in normal subjects occurring 10 hours after oral administration. In 13 normal subjects the plasma activity ranged from 0·23 to 1·71% of the dose per litre of plasma, with a mean of 0·8%, while in 4 patients with pernicious anaemia the level never rose above 0·12%. The authors note that the plasma levels appear low compared with the higher absorption level suggested by urinary and faecal excretion figures. *Janet Vaughan*

919. Radioactive Vitamin B_{12} Absorption Studies: Results of Direct Measurement of Radioactivity in the Blood

A. DOSCHERHOLMEN and P. S. HAGEN. *Blood* [*Blood*] **12**, 336–346, April, 1957. 2 figs., 14 refs.

The absorption of vitamin B_{12} (cyanocobalamin) labelled with radioactive cobalt (^{60}Co) after its oral administration has been investigated at the Veterans Administration Hospital, Minneapolis, by the direct measurement of radioactivity in the blood. Radioactive vitamin B_{12} of a specific activity of 1,082 μc. per mg. was used, doses of 0·46 μg. (0·5 μc.) giving reliable results, although higher counts were obtained with 0·92 μg. Plasma gave higher values than whole blood, 20-ml. specimens of each being counted in a well-type scintillation counter. Urinary excretion was studied in 24-hour specimens.

Radioactivity was not usually found in the plasma until 5 hours after the tracer dose had been given, and a peak was reached after 8 to 12 hours. This is in marked contrast to the rapid rise in the serum values obtained by microbiological assay after massive oral dosage, suggesting different mechanisms of absorption after administration of physiological amounts of the vitamin and after massive dosage. The slow rise in the plasma value (and other related observations such as the fact that 5 to 6 times as much radioactivity was excreted in the urine on the second day than was circulating at the peak) would most readily be explained by a slow passage of the vitamin through the intestinal wall and a gradual release into the blood stream. There was a good correlation between the results of the direct measurement of blood vitamin-B_{12} activity and those of the urinary excretion technique. A clear differentiation was obtained between 9 patients with pernicious anaemia and 36 control subjects. *R. B. Thompson*

920. A Modified Urinary Excretion Test for Measuring Oral Cobalt^{60} Labelled Vitamin B_{12} Absorption and Its Application in Certain Disease States

A. MILLER, H. F. CORBUS, and J. F. SULLIVAN. *Blood* [*Blood*] **12**, 347–354, April, 1957. 1 fig., 13 refs.

The advantages of the urinary excretion test for the measurement of absorption of radioactive vitamin B_{12} (cyanocobalamin) are stressed and the factors influencing the results discussed. In investigations carried out at the Veterans Administration Hospital, Boston, the highest urinary excretion of radioactive vitamin B_{12} after an oral test dose was obtained by giving 2 "flushing" doses, each of 1 mg., of the non-radioactive vitamin intramuscularly 3 and 24 hours respectively after the oral test dose. Vitamin B_{12} labelled with radioactive cobalt (^{60}Co) of specific activity 1·08 μc. per μg. was used, 0·48 μg. (0·52 μc.) being administered as the oral test dose. By this method a better separation of urinary excretion values could be obtained than by the more usual technique of giving a single flushing dose.

A temporary decrease in urinary vitamin excretion to levels similar to those in pernicious anaemia was found in 5 patients with acute infections and in one with severe uraemia. Delayed excretion, but a normal total, was found in 2 out of 3 cases of mild to moderate uraemia. It seems likely that certain other general diseases may be responsible for low excretion values. While high urinary excretion values provide reliable evidence against deficient vitamin-B_{12} absorption, a low value may be due to normal variation, systemic disease, or faulty technique. In patients suspected of having subacute combined degeneration without anaemia values up to 15% of the oral dose, approaching those found in certain systemic diseases, were obtained. *R. B. Thompson*

921. Reduced Effect of Heterologous Intrinsic Factor after Prolonged Oral Treatment in Pernicious Anaemia

M. SCHWARTZ, P. LOUS, and E. MEULENGRACHT. *Lancet* [*Lancet*] **1**, 751–753, April 13, 1957. 5 refs.

At the Bispebjerg Hospital, Copenhagen, the gradual relapse of certain patients with pernicious anaemia during oral treatment with vitamin B_{12} (cyanocobalamin) and intrinsic factor has been investigated by measuring the urinary excretion of vitamin B_{12} labelled with radioactive cobalt (^{60}Co) during the 24 hours after the administration of an oral dose of 0·5 μg. (0·1 μc.) of the labelled vitamin, followed in 2 hours by an intramuscular injection of 1 mg. of non-radioactive vitamin B_{12}. In previous tests

with this technique healthy subjects excreted 10 to 38% of the dose and patients with pernicious anaemia 0 to 8% (indicating failure of absorption).

Four untreated patients with pernicious anaemia were given doses of 25 to 400 mg. of dried hog pyloric mucosa with the test dose of labelled vitamin B_{12}. The proportion of the test dose excreted increased rapidly with the dose of the mucosal preparation up to about 100 mg. and then more slowly, being about 23% with a dose of 400 mg. Two patients who had been treated with vitamin B_{12} or liver extract parenterally for years showed similar responses to the administration of hog pyloric mucosa. Of 9 patients who had had oral treatment with vitamin B_{12} and hog pyloric mucosa for 6 months to 4 years, 7 showed much smaller responses to the same test, 3 excreting less than 5% of the tracer dose after a dose of 400 mg. of hog mucosa; 3 of these patients were slowly relapsing. Another (highly purified) preparation of intrinsic factor from hog pyloric mucosa, of which 2 mg. gave a maximal response in untreated patients or those treated by injection, was not effective in these patients in a dose of 4 mg. Six of the orally treated patients with poor absorption were then tested with 100 ml. of human gastric juice as the source of intrinsic factor, when their responses were as good as those of 3 untreated patients. Neutralized human gastric juice was equally effective. On the other hand the addition of pepsin and hydrochloric acid to the hog pyloric mucosa preparation did not increase its effectiveness.

The possibility is suggested that the intramural "intestinal acceptor" postulated by Glass *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1954, **86**, 522) "is affected by long-term treatment with heterologous intrinsic factor".

G. C. R. Morris

922. **Treatment of Chronic Granulocytic Leukemia with Myleran**

A. UNUGUR, E. SCHULMAN, and W. DAMESHEK. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 727–734, April 18, 1957. 5 figs., 30 refs.

"Myleran" (busulphan) was tried in the treatment of 35 patients (19 male and 16 female) with chronic granulocytic leukaemia, of whom 17 had had previous treatment. The initial dose was 8 to 16 mg. daily, which produced a good response in all patients. There was considerable clinical improvement and the spleen was much reduced in size, in 16 patients regressing completely under the costal margin. The fall in the leucocyte count was maximum by the 4th week. When the count fell to half the initial level the dose was reduced by half, and when a level of 20,000 to 30,000 cells per c.mm. was reached it was reduced to 2 mg. daily; thereafter a maintenance dose of 1 to 2 mg. daily was given with the aim of keeping the count at about 5,000 to 8,000 per c.mm. If the level fell below 6,000 per c.mm. the drug was temporarily withdrawn.

The authors note that the differential leucocyte count also became normal in most patients except for a slight basophilia. The erythrocyte count and haemoglobin level both rose and the platelet count became normal or a little low. The marrow was normal or nearly so in most of the patients examined after varying periods of treatment. No general toxic effects were observed, but in 2 patients thrombocytopenia developed after 240 and 360 days respectively; the drug was stopped and both recovered without incident. One patient developed a pancytopenia with depression of bone marrow after receiving 670 mg. of busulphan in 5 months; he too recovered after treatment with blood transfusion and cortisone. Six patients died in myeloblastic crisis after mean periods of 12·6 months after the beginning of treatment and 31 months after the apparent onset of the disease; this mortality is not regarded as excessive. It is concluded that busulphan affords very satisfactory treatment in leukaemia and has advantages over *x*-ray therapy.

M. C. G. Israëls

923. **A Clinical Study in Hodgkin's Disease**

B. LEVINSON, B. A. WALTER, M. M. WINTROBE, and G. E. CARTWRIGHT. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 519–535, April, 1957. 6 figs., 42 refs.

The natural history of Hodgkin's disease, the effects of treatment, and the prognostic significance of various manifestations of the disease were studied in 91 patients seen at the University of Utah Hospitals, Salt Lake City, between 1945 and 1955. Age at onset of symptoms ranged from 2 to 68 years of age, but in most cases was between 30 and 34. On the average females developed the disease 4 to 6 years earlier than males, but males were affected about twice as often as females. The commonest haematological abnormalities before treatment were a raised erythrocyte sedimentation rate, an increase in the neutrophil count, and anaemia; monocytosis, eosinophilia, and lymphopenia were not uncommon, but leucopenia was present in only 5 patients, and lymphocytosis in one.

In regard to treatment there was no significant difference between the degree or duration of remission in those given *x*-ray therapy, those treated with mustine or tretamine, or those given a combination of the two forms of treatment. The median survival time was 43 months, and 35% of the patients survived for 5 years. There was "suggestive" statistical evidence that females survived longer than males, perhaps owing to the disease being more localized in type. There was no evidence that the early institution of therapy prolonged life. Infiltration of the skin, leucopenia before therapy, and moderate anaemia before or after therapy were signs of ill omen, resulting in an average survival time of 7 months or less. Bone involvement was also a late sign. Involvement of the lung parenchyma was followed by death in about one year; in contrast, pruritus and mediastinal involvement were not considered bad prognostic signs, patients with these complications having a mean survival time of about 2½ years; pruritus was more common in females. Some interesting relationships were noted between various manifestations of the disease: thus all 5 patients with leucopenia had moderate anaemia and splenomegaly, while of 45 patients with splenic involvement, 37 had fever which could not be attributed to infection; no correlation was noted between eosinophilia, pruritus, and skin infiltration.

T. B. Begg

Respiratory System

924. **The Anatomy of Phrenic Nerve Termination and the Motor Innervation of the Diaphragm**
G. S. M. Botha. *Thorax* [*Thorax*] **12**, 50–56, March, 1957. 7 figs., 25 refs.

This paper from the Queen Elizabeth Hospital, Birmingham, describes the nerve supply of the diaphragm with particular reference to the region of the oesophageal hiatus. Numerous dissections were performed at necropsy, and 50 diaphragms were removed from the body and dissected after fixation. The phrenic nerve was found to divide at a variable distance above the diaphragm into 2 to 7 branches. The postero-medial branch was usually the largest, was absolutely constant, and constituted the sole motor nerve supply to the crura. All muscle to the right of the oesophageal hiatus was supplied by the right phrenic nerve, and all that to the left of the hiatus by the left nerve. Nerve fibres also reached the diaphragm from the intercostal nerves, the coeliac plexus, and the sympathetic and splanchnic trunks.

The diaphragms of a number of animals, including rats, ferrets, rabbits, cats, dogs, and monkeys, were also examined, and the nerve supply was found to be very similar to that in man. The postero-medial branch was large and supplied the crura almost exclusively. Stimulation of the phrenic nerve in animals caused contraction of the whole of the ipsilateral half of the diaphragm. The left phrenic nerve in a full-grown rabbit was divided; 5 months later at laparatomy there was complete absence of contraction of the left half of the diaphragm, the muscle fibres of which were atrophic.

It is concluded that the phrenic nerve is the sole motor supply of the diaphragm, the other nerves being sensory. The surgical implications of these findings are discussed.

[This paper should be read with care, as there is some confusion in the terminology.] *D. B. Moffat*

925. **Asthmatic Wheezing. Compression of the Trachea and Major Bronchi as a Cause**
E. Dekker and J. Groen. *Lancet* [*Lancet*] **1**, 1064–1068, May 25, 1957. 5 figs., 46 refs.

Whereas it is commonly assumed that asthmatic wheezing is due to spasm or stenosis of the smaller air passages, the authors present evidence that it is at least partly due to narrowing of the trachea and large bronchi. This is suggested by the facts that the noise is heard universally over the chest with a stethoscope and that wheezing can be produced voluntarily even by normal subjects. Both healthy and asthmatic subjects were taught to wheeze voluntarily. Radiographs taken during inspiration, expiration, and wheezing showed narrowing of the trachea and main bronchi in expiration and gross narrowing during wheezing. The same results were obtained during spontaneous asthmatic attacks. In experiments *in vitro* human lungs obtained at necropsy were caused to " breathe " by varying the air pressure in jars in which they were sealed, the trachea being open to the atmosphere. An expiratory pressure of 1 cm. Hg or more produced considerable stenosis by a prolapse of the membranaceous part of the trachea and main bronchi into the lumen. It is postulated that the high intrathoracic expiratory pressure produced by asthmatics similarly constricts the large air passages and is an important factor in the production of bronchostenosis and wheezing.

The authors suggest that these experiments show how breathing exercises can benefit the asthmatic subject and also throw light on the mechanism of production of so-called psychogenic asthma. *D. Goldman*

926. **Status Bronchospasticus of Non-allergic Origin**
A. L. Banyai. *Diseases of the Chest* [*Dis. Chest*] **31**, 432–436, April, 1957.

927. **Bronchial Involvement in Pulmonary Sarcoidosis**
V. V. Kalbian. *Thorax* [*Thorax*] **12**, 18–23, March, 1957. 5 figs., 8 refs.

In an attempt to determine the frequency of bronchial disease in pulmonary sarcoidosis and to assess the diagnostic value of bronchoscopy 11 cases of pulmonary sarcoidosis seen at Milford Chest Hospital, Godalming, Surrey, were examined by bronchoscopy and biopsy specimens taken of the bronchial mucosa and the scalene node or other lymph node. Acceptance of the cases for inclusion in the investigation depended on finding a typical histological pattern and the absence of tubercle bacilli. All the patients had lung involvement and some had mediastinal lymph-node enlargement.

The most striking change in the bronchi consisted in a granular and rough mucosa (4 cases), while a swollen and thickened mucous membrane was seen in 2 and in 2 others (including one of the four) the bronchi were distorted by the external pressure; no bronchoscopic abnormality was seen in the remaining 4 cases. The bronchial biopsy specimens showed either Langhans cells or non-caseating tubercles in 6 cases, but only a thickened mucosa in 4 others and a normal mucosa in one. It was in the bronchi with a granular appearance that tubercles were most likely to be found. In 7 out of 9 biopsy specimens of the scalene node non-caseating tubercles were present. The author believes that bronchoscopy, together with examination of a biopsy specimen, can be of considerable diagnostic help in sarcoidosis. He also stresses the value of excising the scalene node, since it is so frequently involved in the disease.

This paper contains a review of the literature on bronchial sarcoidosis and a number of illustrations.

Paul B. Woolley

928. **Broncholithiasis.** (Бронхиальный камень)
I. G. GRISHIN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **35**, 151–152, No. 2, Feb., 1957. 6 refs.

The case is described of a woman of 42 who complained of general weakness, cough with slight mucoid sputum, and a feeling of constriction in the chest, especially on the right side. For 7 years she had suffered from chronic pneumonitis associated with bronchiectasis. On examination it was found that the right side of the thorax did not move with respiration. There was impaired resonance over the lower chest on the same side, with weak breath-sounds and vocal fremitus, while soft crepitations were audible on auscultation. The antero-posterior radiograph showed a triangular area of intense infiltration in the right lower lobe measuring 3×4 cm., and the lateral view also showed a triangular opacity, suggestive of segmental atalectasis. The sputum contained no tubercle bacilli or elastic fibres.

Three weeks after admission the patient had some severe bouts of coughing, in one of which she expectorated a small stone covered with blood, followed by 100 ml. of bloody, purulent sputum. After this the general condition improved, the temperature fell to normal, and further radiography showed that the triangular shadow in the right lung had disappeared. The stone was rounded in form and greyish-white in colour; the surface was rough. It measured 1·2×0·7 cm. and weighed 0·53 g. On section it was porous. Spectral analysis showed the presence of magnesium, sodium, calcium, and phosphorus, with small traces of other elements. The patient received 10 mega units of penicillin intramuscularly and 5 inhalations of an aerosol of the same antibiotic. She was discharged in good condition 2 weeks after coughing up the stone.

L. Firman-Edwards

929. **Bronchiectasis in the Aged**
J. B. ANDOSCA. *Diseases of the Chest* [*Dis. Chest*] **31**, 585–592, May, 1957. 4 figs.

930. **Stenosing Non-caseating Tuberculosis (Sarcoidosis) of the Bronchi**
K. M. CITRON and J. G. SCADDING. *Thorax* [*Thorax*] **12**, 10–17, March, 1957. 14 figs., 13 refs.

The authors describe in considerable detail the clinical histories of 3 patients with multiple strictures of the bronchi thought to be due to a granulomatous process of sarcoidotic or non-caseating tuberculous type who were seen at the Brompton Hospital, London. Cough and sputum, together with wheezing and severe dyspnoea, were almost constant symptoms, whereas the most important physical sign in the lungs was a " soft inspiratory and expiratory stridor ". Radiologically, areas of collapse were seen in different zones of the lungs due, presumably, to plugging of the bronchi. The bronchograms showed narrowing of the main bronchi and the proximal segments of the secondary bronchi. Bronchoscopically, the appearances varied considerably; the mucosa might be swollen and red or contain granulation tissue, and in the later stages fibrotic changes with stenosis were seen. The authors did not find that antituberculous drugs had much effect on the clinical picture, but the addition of cortisone brought about considerable subjective improvement.

In a discussion of the aetiology of the condition they base their diagnosis of sarcoidosis on the findings revealed by histological examination of biopsy specimens. They believe that these 3 cases, like most cases of sarcoidosis in Great Britain, were of tuberculous origin. The paper concludes with a short review of the literature on sarcoidosis of the bronchi, and there are some good photomicrographs of the histological and radiological changes.

Paul B. Woolley

931. **Involvement of the Thoracic Wall in Bronchogenic Carcinoma. Study of 16 Cases in which Pneumonectomy or Lobectomy and Simultaneous Resection of the Thoracic Wall Were Done**
Y. K. J. GRONQVIST, O. T. CLAGETT, and J. R. MCDONALD. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 487–495, April, 1957. 3 figs., 14 refs.

932. **Surgical Treatment of Large Air Cysts of the Lung**
L. H. CAPEL and J. R. BELCHER. *Lancet* [*Lancet*] **1**, 759–762, April 13, 1957. 2 figs., 12 refs.

Air cysts of the lung are not common. They may be small or large, and either group may or may not be associated with symptoms of breathlessness. When breathlessness is present it is often difficult to determine what proportion of the complaint is due to the cyst and what due to the associated emphysematous disease of the lungs and bronchitis. Diagnosis is best made radiographically, and the authors emphasize the importance of fluoroscopy in the assessment of these patients. Bronchograms are sometimes of value in outlining the limits of a cyst and in distinguishing the latter from a pneumothorax.

Results are reported in 21 cases of large air cysts of the lung selected for operation on account of breathlessness. A variety of surgical procedures were carried out. In 2 cases the cyst was removed intact after ligation of its blood supply; in 10 cases a formal resection was performed; in 8 cases the visceral pleura overlying the cysts was excised and the air leaks thus exposed were closed by ligation; in one case tube drainage was employed. Pulmonary autonomic denervation was not performed on any of the patients.

One patient died 4 days after operation from pulmonary insufficiency; 3 other patients died subsequently —2 from unrelated causes and one from a contralateral spontaneous pneumothorax. Nine of the patients were enormously improved; in all of these the cyst had occupied more than half the lung field. Improvement of those with less extensive cysts was less striking. Clinical improvement has in the majority of cases been accompanied by improvement in the vital capacity, maximum breathing capacity, and timed ventilation readings. However, later measurements of the timed ventilation showed a significant but unexplainable fall.

[This paper emphasizes the important part that surgery has to play in this condition even when the disability is very severe.]

W. P. Cleland

Urogenital System

933. **L-Noradrenaline Therapy in Acute Renal Failure**
D. MATTINGLY. *Lancet* [*Lancet*] **1**, 962–966, May 11, 1957. 3 figs., 18 refs.

It has been shown by various workers that doses of noradrenaline sufficiently large to raise the systolic blood pressure of normal individuals by 25 to 50 mm. Hg produce intrarenal vasoconstriction and relative tubular ischaemia, while Lathem (*J. clin. Invest.*, 1956, **35**, 1277) has demonstrated similar effects in patients with chronic renal disease. However, in hypotensive patients restoration of the systolic pressure to a normal level by means of noradrenaline would tend to increase the renal blood flow, and the present author suggests that this increase more than compensates for the local vasoconstrictor action on the renal vessels. He reports the successful treatment of 2 patients with peripheral circulatory failure and impaired renal function by means of this drug at the Royal Devon and Exeter Hospital.

In the first case a fit woman aged 63 years with no history of renal disease underwent a vaginal hysterectomy, during which she received a transfusion of 2 pints (1·14 litres) of compatible whole blood. The next day no urine was passed and she commenced to vomit. Fluid intake was restricted to 1 litre of distilled water containing 400 g. of dextrose, administered by intragastric drip. On the 2nd day only 350 ml. of urine was collected by catheter. Daily injections of 1 mega unit of crystalline penicillin were begun (subsequently supplemented by erythromycin by mouth). That night profuse watery diarrhoea occurred and continued throughout the 3rd day, during which signs of peripheral circulatory failure, with an unrecordable blood pressure, developed. The patient was clinically dehydrated and failed to respond to the rapid infusion of 2 litres of physiological saline and 2 pints of plasma and to 25 mg. of methylamphetamine given intravenously. Noradrenaline was then added to the infusion and immediately the systolic pressure rose to 130 mm. Hg. By adjustment of the dosage of noradrenaline and rate of infusion it was subsequently maintained at approximately this level for 86 hours without any complications or side-effects. On the 4th day the amount of noradrenaline required to maintain the systolic blood pressure (which had risen to 73 μg. per minute) began to fall and was only 4 μg. per minute on the 7th day, when it was discontinued. Oliguria persisted until the 11th day, after which the blood urea level, having risen to a maximum of 320 mg. per 100 ml. on the 10th day, rapidly fell to normal.

The second case was that of a male diabetic aged 49 years who was admitted in a drowsy and confused state with diabetic ketosis and a blood sugar level of 800 mg. per 100 ml. He failed to respond to massive doses of insulin and intravenous saline, becoming pulseless and oliguric, with a blood urea level of 160 mg. per 100 ml. A drip infusion containing noradrenaline restored the systolic blood pressure to 130 mm. Hg and it was maintained at this level with a dosage of 20 μg. of noradrenaline per minute. He recovered completely, having received 3,200 units of soluble insulin and 12 litres of intravenous fluid during the first 12 hours of treatment.

The author suggests that "the only real criterion of effective dosage [of noradrenaline] is the fairly rapid rise of the systolic pressure, within a few minutes, to about 130 mm. Hg". Lack of response should be met by doubling or trebling the concentration of noradrenaline in the infusion rather than by increasing the rate of infusion, so as to avoid overhydration. He also recommends that noradrenaline should be given in 5% dextrose or dextrose–saline solution, as it breaks down in an alkaline medium. If saline, blood, plasma, or antibiotics are to be given intravenously they should be injected into another vein. *L. G. Fallows*

934. **Postural Adjustments and Protein Excretion by the Kidney in Renal Disease**
S. E. KING. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 360–377, Feb., 1957. 2 figs., 27 refs.

The author describes studies carried out on 27 young males with proteinuria at the Renal Research Laboratory, Governors Island, New York. There were 9 cases of chronic proteinuria of undetermined origin, 9 of chronic glomerulonephritis with mild proteinuria, 3 of chronic glomerulonephritis with severe proteinuria, 2 of subsiding acute nephritis, 3 of pyelonephritis, and one of the nephrotic syndrome. In 14 cases the inulin and PAH clearances and protein excretion rate were estimated after fluid, salt, and protein restriction for 12 hours to ensure a relatively constant urine flow. Clearances were determined in the supine position and in the erect lordotic or erect kyphotic or tilt positions. In 13 patients under a similar dietary regimen only the rates of protein and sediment excretion were estimated in the supine and standing positions. The procedures were discontinued if postural hypotension or syncope occurred, and in the second group urine specimens of low specific gravity and those not showing decreased volume on standing were discarded. Control clearance studies were carried out on 20 normal subjects. In one patient with mild chronic glomerulonephritis the effect of raising glomerular pressure by the intravenous injection of L-noradrenaline was investigated.

No uniform effect on the protein excretion rate resulted from changes in posture; although the protein excretion rate usually increased on orthostasis, the mean increase for the whole group was doubtfully significant. However, when patients with an initial proteinuria exceeding 1 mg. per minute and those who developed syncope were excluded, the increase in the protein excretion rate became very significant. Similarly, excluding patients with syncope, urinary protein concentration increased significantly with standing in cases with initially mild

proteinuria but not in those with severe proteinuria. Both the glomerular filtration rate and the renal plasma flow were significantly reduced on standing, and the filtration fraction was significantly increased.

The author points out that the estimation of protein concentration, which is dependent on alterations in urinary volume, is of less value than the estimation of the protein excretion rate. The part played by pores in the glomerular membrane in allowing the passage of protein molecules in varying conditions is discussed with particular reference to changes in glomerular pressure induced by changes in posture and also by the experimental infusion of L-noradrenaline, which caused a similar increase in the rate of protein excretion.

L. Capper

935. **A Comparative Study of Functional and Morphological Renal Changes in Glomerulonephritis.** [In English] J. BROD and D. BENEŠOVÁ. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 23–32, 1957. 6 figs., 21 refs.

Although our knowledge of the structural changes in the kidneys in the final stages of glomerulonephritis is adequate, that of the changes in the early stages is still incomplete. At the Institute for Cardiovascular Research, Prague, denervation and decapsulation of the kidney carried out during the last 5 years on 38 patients for therapeutic purposes gave the authors the opportunity to compare *in vivo* the morphological changes of active disease in the glomeruli and tubules with the results of a number of renal function tests, including the quantitative estimation of the urinary excretion of erythrocytes, leucocytes, and casts over 24 hours, the renal urinary concentrating power, and the erythrocyte sedimentation rate.

Although there was no satisfactory correlation between the morphological changes and any one of these tests singly it was noted that if at least three of the tests were abnormal it was highly probable that histological evidence of active disease would be found in the biopsy specimen. A raised blood pressure was almost invariably associated with a creatinine clearance of less than 50 ml. per minute, but it was not related to morphological evidence of active disease or even constantly associated with fibrinoid necrosis of the vascular walls.

Robert Mahler

936. **Parenteral Administration of Reserpine in the Treatment of Hypertension Due to Acute and Chronic Nephritis. Clinical and Renal Hemodynamic Studies**
C. W. DAESCHNER, J. H. MOYER, W. R. BELL, and J. L. CLARK. *Pediatrics* [*Pediatrics*] **19**, 566–579, April, 1957. 5 figs., 4 refs.

The effect of reserpine on the blood pressure, glomerular filtration rate, and renal plasma flow was studied in 44 children with acute and 6 with chronic nephritis, and in 5 children without nephritis, at the Jefferson Davis City–County Hospital, Houston, Texas. Administration was by intramuscular or intravenous injection in doses of 20 to 200 μg. per kg. body weight (usually 80 to 150 μg. per kg.). In the 5 children without nephritis there was a slight but not significant fall in blood pressure, but there was a decrease of effective renal blood flow. In 22 patients with acute nephritis the higher the diastolic blood pressure initially, the greater the fall produced by reserpine; the maximum effect occurred in about 2 hours and persisted for 12 to 18 hours or more. Immediately after the hypotensive effect in 11 patients with acute nephritis whose renal function was studied there was a fall in effective renal blood flow to an average of 73% of the control value, but this began to rise during the next 1 to 1½ hours. These changes were not, however, statistically significant. In 6 patients with chronic nephritis, in all of whom the diastolic pressure before treatment was higher than 130 mm. Hg, there was an average decrease of mean blood pressure (diastolic pressure plus one-third of the pulse pressure) of 47 mm. Hg. This fall in the mean blood pressure was accompanied by a slight decrease in effective renal blood flow.

It is concluded that reserpine given parenterally is safe and effective in the control of hypertension in acute or chronic nephritis in childhood.

C. Bruce Perry

937. **The Natural History of Nephrosis**
R. M. TODD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 99–105, April, 1957. 5 figs., 20 refs.

The author reports his experience of the nephrotic syndrome of unknown aetiology as seen at Alder Hey Children's Hospital, Liverpool, during the period 1948–55 in 32 patients (21 male, 11 female) of whom 11 were under 3 years of age, 14 between 4 and 7 years, and 7 over this age. The onset was insidious, and in 2 cases was related in time to immunizing injections against diphtheria. In all cases such typical features as gross oedema, heavy proteinuria, and a normal or only slightly elevated blood urea level were noted at the onset of illness. Electrophoretic patterns of plasma proteins, studied in 6 patients, showed diminished γ-globulin and increased α_2-globulin values.

The course of the illness could not be predicted, its duration varying from 3 months to 5½ years in those who eventually appeared to recover, and from 6 weeks to 7½ years in the fatal cases. One patient after an attack of measles had a complete remission lasting 2 years. Treatment, which was conventional, included the administration of ACTH or cortisone in 17 cases, of which the oedema was unaffected in 3, was lessened in 8, and worsened in 6, but in 3 of these last diuresis occurred on stopping the hormone treatment. In all, 11 patients died, 14 are cured or in remission (for over one year in 9 cases), one was lost sight of, and the disease is still active in 6. From a study of the literature the author concludes that the recovery rate is about 50% and that too gloomy an outlook has been taken in the past. Post-mortem examination, performed in 7 cases, revealed contracted, granular kidneys of "chronic nephritis" in 3 cases which had been characterized by the long duration of the illness (5 to 7 years), with hypertension and uraemia terminally. The other 4 cases showed changes characteristic of Ellis's Type-2 nephritis and in these the illness had been of short duration (14 weeks to 8 months), with normal blood pressure and absence of uraemia.

K. G. Lowe

Endocrinology

938. **Preliminary Experiences with Transplants of Cultured Parathyroid Tissue in Hypoparathyroidism**
R. F. Escamilla, C. H. Kempe, J. Crane, L. Goldman, and G. S. Gordan. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 649–661, April, 1957. 2 figs., 11 refs.

Previous methods of transplanting parathyroid tissue into patients with hypoparathyroidism are briefly reviewed and evaluated. Following the pioneer methods of Gaillard the authors, working at the University of California School of Medicine, San Francisco, first used parathyroid glands derived from stillborn infants or infants who died soon after birth; later, tissue from benign parathyroid adenomata was used. The tissue was maintained by tissue-culture methods and gradually adapted to the recipient's serum by means of successive transfers from the sixth day onwards. Implantation into the 11 recipients was made between 12 to 15 days later because after that time fibrous tissue begins to encapsulate the culture. The nutrient media employed are described in detail.

In one case refractory to antitetany therapy, 26 pieces of culture were implanted in the sheath of the axillary vein, resulting in definite improvement which persisted for 9 months; a second implant of 45 pieces of adenomatous tissue resulted in further but less marked improvement which persisted for another 13 months. In 13 other cases from 13 to as many as 80 fragments were implanted; in one of these some measure of improvement appeared to last for 19 months. In a further 6 cases brief improvement of one to 6 weeks occurred, but in the 3 remaining cases no apparent improvement was noted. Only the first 2 cases were regarded as definite " takes ". *C. L. Cope*

THYROID GLAND

939. **The Heart in Hyperthyroidism: Effect of Antithyroid Drugs and I^{131}**
J. P. Murphy and D. L. Sexton. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **5**, 109–116, Feb., 1957. 5 figs., 6 refs.

In support of the belief that hyperthyroidism can cause cardiac disturbance in the absence of organic heart disease, 3 such cases are described from St. Louis University School of Medicine, Missouri.

In the first case, in a woman aged 40 who had previously been treated with antithyroid drugs, subtotal thyroidectomy on two occasions, and local thyroid irradiation, atrial fibrillation and congestive cardiac failure developed with a recurrence of thyrotoxicosis. Preliminary treatment with digitalis, diuretics, and methimazole was followed by three doses of radioactive iodine (^{131}I) given over 6 months. Spontaneous reversion to sinus rhythm occurred, with relief of cardiac failure even although the digitalis was withdrawn when the patient became euthyroid. The second patient, a man aged 47, had auricular fibrillation, congestive cardiac failure, and thyrotoxicosis. Similar treatment to that described above was followed by three doses of ^{131}I given over a 4-year period. In this case adequate cardiac compensation occurred when the patient was euthyroid, but atrial fibrillation persisted. The third patient, a women aged 47, after a prolonged course of propylthiouracil, was treated with ^{131}I for recurrence of toxicity, no cardiac involvement being evident at this time. One month later she developed a fatal thyroid crisis accompanied by atrial fibrillation and congestive failure. Postmortem examination showed hypertrophy of the heart and histological changes in the myocardium.

The authors suggest that before beginning treatment with ^{131}I all cases of thyrotoxicosis should be given a course of antithyroid drugs, with digitalis and diuretics as well if cardiac failure is present or imminent.
Gerald Sandler

940. **Treatment of Metabolic Insufficiency and Hypothyroidism with Sodium Liothyronine. Preliminary Report**
E. M. Fields. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 817–821, March 9, 1957. 15 refs.

The clinical effects of sodium liothyronine (L-triiodothyronine) were studied in 100 children and adolescents aged between one and 18 years, 60 of whom suffered from hypothyroidism and 40 had a diagnosis of metabolic insufficiency. Of the 60 hypothyroid children results were classified as excellent (relief of 90% or more of symptoms) in 35, good (relief of 70 to 90% of symptoms) in 22, fair (at least 50% of symptoms relieved) in 2, and poor (less than 50% relief) in only one. Results in the groups with metabolic insufficiency were: excellent, 22; good, 15; and fair, 3. None of the patients in either group developed side-reactions. It is concluded that administration of triiodothyronine is an effective and safe form of treatment for these conditions in children.
C. L. Cope

941. **Carcinoma of the Thyroid. A Review of 100 Cases**
R. Kilpatrick, G. W. Blomfield, F. E. Neal, and G. M. Wilson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **26**, 209–233, April, 1957. 9 figs., bibliography.

The authors have reviewed the 100 cases of carcinoma of the thyroid gland—20 in men and 80 in women—referred to the Sheffield National Centre for Radiotherapy since 1946. Histological proof of the lesion was obtained in 78 cases and in 22 there was strong clinical evidence of carcinoma because of local or metastatic recurrence. After analysing the clinical features in detail the authors stress the fact that in many cases of thyroid disease which later prove to be malignant a clinical diagnosis

of cancer of the thyroid cannot be made. The commonest histological type (45%) was papillary carcinoma, which showed a lower age incidence than the other groups, 16 cases being in patients under 40 years of age, whereas all but 2 of the remaining patients in the series were over that age. Small- or large-cell types accounted for 30% of the tumours, and 23% were follicular.

Most of the patients were treated by deep *x*-ray therapy, alone or after operation; 11 were treated by operation alone and 6 with radioactive iodine, while 5 received no treatment. The 5-year survival rate was 73·5% for papillary carcinoma and 16·7% for undifferentiated types, while the rate for follicular carcinoma was intermediate between these.

The authors review the literature on the possible relationship between simple goitre and the subsequent development of thyroid carcinoma, and conclude that there is strong evidence against any such connexion. Only 18% of the present series of patients had a pre-existing goitre, while coexisting hyperthyroidism was also a rare occurrence, being found in only 7 patients. The possible relationship between previous irradiation and the development of thyroid cancer is also discussed. In 3 out of 8 cases of thyroid cancer developing before the age of 35 there was a history of irradiation of the neck in childhood, no such history being obtained from any of the older patients. *D. G. Adamson*

ADRENAL GLANDS

942. **Management of Chronic Adrenocortical Insufficiency with Oral Replacement Therapy**
J. A. Epstein and H. S. Kupperman. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 5, 117–121, Feb., 1957. 10 refs.

After a brief review of the development of mineralocorticoid replacement therapy in adrenal insufficiency the authors report the results obtained with 9-alpha-fluorohydrocortisone given orally in 5 cases of primary and 3 cases of secondary chronic adrenal insufficiency under treatment at New York University–Bellevue Medical Center, New York. All the patients received 10 mg. of hydrocortisone twice daily and a normal diet, together with 9-alpha-fluorohydrocortisone in a dose of either 0·1 mg. daily or 0·25 mg. on alternate days. They were followed up for periods of 6 to 20 months.

In 7 cases the patient was well maintained, showed no evidence of muscular weakness or fatigue, and could do a normal day's work. In the 8th case, in a negro woman aged 73 with a 5- to 10-year history of previous hypertension, the drug was discontinued after 5 months because of a significant increase in blood pressure associated with severe headaches; in this case subsequent maintenance therapy was with hydrocortisone alone when the raised blood pressure returned to previous levels. In 2 of the patients with primary adrenal insufficiency pigmentation decreased, probably due to suppression of pituitary corticotrophin by the drug. Clinical signs of overdosage with 9-alpha-fluorohydrocortisone are gain in weight, oedema, and hypertension, and radiology may reveal sudden cardiomegaly. Withdrawal of the drug usually leads to disappearance of toxic manifestations within a week. *Gerald Sandler*

943. **Medical Considerations in Adrenal Surgery**
R. E. Bolinger and M. H. Delp. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 662–677, April, 1957. 4 figs., 44 refs.

The authors describe, from the University of Kansas School of Medicine, Kansas City, their experiences with 17 patients subjected to adrenalectomy, in 8 cases for the relief of Cushing's syndrome, in one each for the adrenogenital syndrome, phaeochromocytoma, and essential hypertension respectively, and in 5 for metastatic carcinoma of the breast or (in one) of the prostate. The symptoms, physical signs, laboratory findings, and management of these cases are reviewed. The authors advocate the administration of potassium chloride for one week preoperatively and of cortisone for 24 hours in cases not showing signs of hypercorticism. The postoperative course is discussed. Extra salt was usually given and in 3 cases deoxycortone was required. They point out that a florid Cushing's syndrome may sometimes be associated with the absence of any significant macroscopic or microscopic changes in the adrenal glands. There were no deaths, but one patient developed serious postoperative metabolic alkalosis and pulmonary oedema, and another severe progressive pigmentation of the skin. *C. L. Cope*

DIABETES

944. **Plasma-insulin and Insulin Resistance**
C. W. Baird and J. Bornstein. *Lancet* [*Lancet*] **1**, 1111–1113, June 1, 1957. 18 refs.

Existing methods of estimating the concentration of insulin in plasma are technically not very satisfactory and may give inaccurate results owing to the presence and continued activity of insulin antagonists in the plasma. As the first stage in the development of a more satisfactory method of assay the authors, working at the University of Melbourne, set out to concentrate the insulin from the plasma and to separate it from the plasma glucose. During this fractionation they hoped that the antagonists might be destroyed or separated from the insulin, although they could take no specific measures directed to this end. The method finally adopted is described in detail. It involved repeated extraction of fresh plasma with a solvent mixture and the precipitation of the protein content of the combined extracts. This proteinous extract contained no glucose. Assay of the extract and of the residue by the rat-diaphragm technique showed that all insulin-like activity was contained in the extract. Confirmation that the insulin-like effect was due to insulin was obtained by demonstrating the loss of this activity after treatment with alkali or with cysteine. It was found that extract derived from plasma to which insulin labelled with radioactive sulphur had been added contained 85% of the radioactivity.

The method was then applied to the examination of plasma from healthy and from diabetic subjects. In all cases in which the crude plasma showed insulin activity, such activity was also demonstrable in the concentrated extract. In the normal subjects, the degree of activity was similar in the crude plasma and in the extract. Diabetics who had not recently received treatment with insulin fell into two groups: (1) those whose plasma contained insulin activity within the normal range, and (2) those without detectable insulin in the plasma. The crude plasma of patients in diabetic coma showed either no acceleration or, in many cases, actual inhibition of glucose uptake by the rat diaphragm. However, examination of the extracts prepared from the same plasma samples revealed that in the majority insulin was present. On examination of the residue from the extraction process in these latter cases, inhibition of glucose uptake by the rat diaphragm was observed in some cases, while in others the insulin antagonists appeared to have been destroyed by the fractionating process. *H.-J. B. Galbraith*

945. **Carbutamide and Plasma Insulin Activity**
C. VON HOLT, L. VON HOLT, J. KRACHT, B. KRÖNER, and J. KÜHNAU. *Science* [*Science*] **125**, 735–736, April 19, 1957. 17 refs.

It has been supposed that carbutamide acts by inhibiting the production of glucagon, but the authors have shown that the morphological appearance of the islets of Langerhans and the known metabolic effects of the drug are not in agreement with such a mechanism. The effect of single and daily oral doses of carbutamide on plasma insulin activity was therefore studied at the University of Hamburg in rats. Insulin activity was determined by measuring the increase in glycogen synthesis in the isolated rat diaphragm using the anthrone method of Seifter *et al.*, the blood sugar concentration being determined before administration of the drug and again at the time of insulin determination.

The results showed a significant rise in plasma insulin activity after a single dose of carbutamide, together with a decrease in blood sugar level. After daily doses of carbutamide for 3 months, however, these effects were no longer apparent. It is therefore considered that initially carbutamide stimulates the activity of the β cells of the islets of Langerhans, but that this is followed by β-cell insufficiency on prolonged stimulation. Thus not all the metabolic effects of the drug can be explained in terms of increased insulin output. *F. W. Chattaway*

946. **Insulin Deficiency and Diabetes.** [In English]
F. GERRITZEN, E. L. NOACH, M. VAN WIJHE, and L. E. M. VALK. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **25**, 91–100, May, 1957. 2 figs., 15 refs.

In a search of the literature the authors have been able to find only slender evidence that the later complications of diabetes are due to insulin deficiency, with the possible exception of diabetic cataract. They therefore attempted, in experiments at the University of Leiden, Holland, to induce such complications in rats made insulin-deficient by means of alloxan. Animals in which glycosuria lasted for only the first week of alloxan treatment were used as controls. The experiment was continued for 323 days, and at the end of this period only 5 glycosuric rats and 3 controls survived. These animals were killed and a number of organs examined microscopically.

Livers and arteries appeared normal. Glycogen was found in the renal tubules of the glycosuric rats but not of the controls. Some cataracts developed, but no micro-aneurysms, nor any ocular change which could be described as a diabetic retinopathy. Thus the investigation is considered as having failed to support the view that, in the rat at any rate, insulin deficiency is responsible for late complications in diabetes. *C. L. Cope*

947. **Modification of Hypoglycaemia with Hexamethonium Bromide**
E. MARLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 921–924, April 20, 1957. 2 figs., 38 refs.

In view of the ganglion-blocking properties of hexamethonium bromide the effect of this drug on the insulin tolerance test was investigated in 24 male schizophrenic patients at Severalls Hospital, Colchester. After a diet containing at least 300 g. of carbohydrate daily for 3 days the tests were performed before and again after administration of 25 to 50 mg. of hexamethonium intramuscularly together with the insulin, in both the recumbent and erect postures. When the patient was recumbent the addition of hexamethonium to small doses of insulin led to an augmented initial fall in the blood sugar level, with a diminished response to hypoglycaemia as indicated by the levels later in the curve. When the patient was erect the induction of syncope was associated with a smaller initial fall in sugar level and a better response to hypoglycaemia. The response to large amounts of insulin (between 480 and 640 units intramuscularly as used in shock treatment) was more rapid and resulted in more profound hypoglycaemia after injection of 100 mg. of hexamethonium intramuscularly. It is emphasized that there appears to be some risk in giving both hexamethonium and insulin to diabetic patients.
Kenneth Gurling

948. **Late Diabetes Mellitus. Diagnostic Considerations**
E. J. CHESROW and J. M. BLEYER. *Geriatrics* [*Geriatrics*] **12**, 171–180, March, 1957. Bibliography.

The authors report the results of screening tests for diabetes on 1,000 patients over the age of 60 at Cook County Institution, Oak Forest, Illinois. In those in whom urine tests and blood sugar estimations, carried out between 2 and 2½ hours after a meal, gave a positive result an oral glucose tolerance test was performed. According to their response to this test the patients were divided into a diabetic and a potential diabetic group, the former being characterized by the presence of hyperglycaemia and glycosuria and the latter by hyperglycaemia without glycosuria. Among the total of 1,000 patients 64 diabetics and 24 potential diabetics were discovered, and the authors present a review of the clinical features of 79 of these cases (60 diabetics and 19 potential diabetics).

The median age was above 70, ranging from 70·3 to 74·4 in the two groups and sexes, and the ratio of men to women was 2·4 to 1. None of the 59 mentally alert diabetic patients able to do so gave a family history of diabetes, but in 40% of them there was a family history of obesity. The frank diabetic symptoms of thirst, polyuria, and polyphagia were relatively uncommon, although weight changes were reported by many patients, one-quarter having noted weight loss, one-quarter weight gain, while 36·7% were overweight and 43% were underweight at the time of diagnosis. Symptoms of neuropathy were present in 36·1% of the diabetics and 41·6% of the potential diabetics, but nocturnal diarrhoea was a feature in only one case. Acetonuria occurred during the glucose tolerance test in 28 patients, but nausea and vomiting in only 3. The blood pressure was above 160/90 mm. Hg in 53·3% of the diabetic and in 31·5% of the potential diabetics, but angina of effort and any signs of cardiac failure were uncommon. No characteristic signs of retinopathy were found in any of the patients, although lens opacities obscured the fundus in some, the incidence of cataract being high (52·8% in the diabetics and 47% in the potential diabetic group).

The authors conclude that a low incidence of primary diabetic symptoms is characteristic of diabetes appearing late in life, and suggest that the absence of late complications such as advanced retinopathy, gangrene, and nocturnal diarrhoea indicated that the diabetic state had only recently developed in the patients studied. In general they found the clinical features in the diabetic and potentially diabetic groups very similar and they therefore urge that even mild deviations from the normal revealed by the oral glucose tolerance test should be taken seriously. In their opinion glycosuria is of less significance than the hyperglycaemia which was common to both groups. *John Lister*

949. **Behaviour Problems in Juvenile Diabetics**
P. KATZ. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 738–743, May 1, 1957. 18 refs.

Emotional disturbances may aggravate diabetes mellitus by a direct effect on metabolic processes or more indirectly by causing a patient to neglect treatment. In childhood emotional difficulties arise from family maladjustment and particularly from faulty attitudes adopted by parents; also the sense of being different from other children and having to submit to the restrictions of treatment may lead to behaviour disorders. Of 26 juvenile diabetics seen during a period of 6 years at the Children's Hospital, Winnipeg, 11 had behaviour problems requiring psychiatric help. Of these 11 children with behaviour problems, 9 refused to follow their diets and 6 used their diabetes to achieve their own purposes, which in the case of one 15-year-old child was to break up the marriage of her mother and stepfather.

[This paper illustrates the importance of proper appraisal and sympathetic handling of personal problems, but the proportion of unruly children is unusually high and not representative of general experience with young diabetics.] *K. O. Black*

GENITAL GLANDS

950. **Increased Erythropoiesis Induced by Androgenic-hormone Therapy**
B. J. KENNEDY and A. S. GILBERTSEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 719–726, April 18, 1957. 1 fig., bibliography.

The authors describe some of the changes caused by androgenic hormones which were used at the University of Minnesota Hospital, Minneapolis, in the treatment of 68 patients with advanced breast cancer. Testosterone propionate, 100 mg. 3 times weekly, was given to 31 patients, stanolone (dihydrotestosterone) in the same dose to 32, and methylstanolone was given orally to 5 patients in doses of 200 mg. daily. Signs of increased erythropoiesis developed in 24 of these patients, the maximum effect being noted on the average 4·8 months (range 2 to 11 months) after the beginning of treatment. The patients complained of flushing and intolerance of heat and often developed an appearance like that in Cushing's disease. [No mention is made of splenomegaly.] The mean haemoglobin level before treatment was 12·9 g. (range 8·6 to 15·6 g.) per 100 ml., which after treatment rose to a mean of 17·6 g. per 100 ml., a significant increase occurring in the first month of treatment. Erythrocyte counts increased in a parallel manner, but no changes were noted in the leucocyte or the platelet count. The bone marrow showed some normoblastic activity, but no change in granulocytes or megakaryocytes. The erythrocyte mass was estimated in 11 patients; in all 11 this value was lower than normal, but 6 of the patients who responded to treatment showed a rise to the normal or in 4 cases above the normal level. The authors then tried the effect of giving cortisone, 300 mg. daily, in addition to the androgen, but although this increased somewhat the haematopoietic effect, there was no added relief for the patient.

Testosterone was also given to 6 patients with various secondary anaemias with good results. For example, when a man aged 64 who was suffering from "myeloid megakaryocytic hepatosplenomegaly" was given testosterone propionate in doses of 100 mg. intramuscularly 3 times weekly for 6 months his haemoglobin level rose from 6·1 to 13·6 g. per 100 ml.; in another patient, a man aged 38 with chronic glomerulonephritis who was similarly treated, the haemoglobin value rose from 8·3 to 14·0 g. per 100 ml. in 5 months. These studies suggest that androgenic hormones are specific stimulants of erythropoiesis.

The authors quote the extensive literature reporting animal studies, observing that clinical reports are, unfortunately, few and not very detailed. They conclude that the treatment of anaemia with testosterone is worth further trial. *M. C. G. Israëls*

951. **Persistence of Urinary Oestrogen Excretion after Oophorectomy and Adrenalectomy**
R. D. BULBROOK and F. C. GREENWOOD. *British Medical Journal* [*Brit. med. J.*] **1**, 662–666, March 23, 1957. 8 figs., 18 refs.

The Rheumatic Diseases

952. **Antistreptolysin-O Determinations in Health and in Disease**
M. SAINT-MARTIN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 627–633, April 15, 1957. 4 figs., 26 refs.

Although the antistreptolysin-O titre is simple to estimate it has not been widely used as a routine estimation, as the results are often difficult of interpretation and it is necessary to know the prevalence of streptococcal infection and the level of antistreptolysin-O titre in the population being investigated. To provide such a baseline for these studies the author, working at the Hôtel-Dieu Hospital, Montreal, first performed this test on the sera of 1,153 presumably normal young adults aged from 15 to 40 years in the Montreal area. Of these, 648 (56·1%) showed a titre below 100 units, and 1,101 (95·5%) a titre below 250 units; thus only 4·5% had titres above 250 units.

The titres of groups of patients with various disorders were then studied. Of 46 cases of active rheumatic fever, only one was found to have a value below 100 units, while in the majority (38 cases) the value was over 250 units, the mean for the group being 665 units. In 72 patients with inactive rheumatic fever the titre was not raised so markedly, although it was still well above the normal range. Lastly, in 32 patients with rheumatoid arthritis and in 108 with miscellaneous diseases the range of titres corresponded quite well with that in the normal subjects. In further studies serial estimations of the antistreptolysin-O titre in the patients with acute rheumatic fever showed two patterns; in both the titre rose initially to a high level for about a month, but thereafter, although it sometimes fell to normal values with clinical recovery, it more often remained at a high level for many months after the disease had become inactive.

The author considers that this test is useful as an indicator of activity in rheumatic fever, and that a low antistreptolysin titre is of value diagnostically in excluding this condition. *B. E. W. Mace*

953. **Changes in the Serum Protein Fractions in Acute Attacks of Gout.** (Modifications des fractions protéiques sériques au cours de l'accès de goutte)
J. GROULADE and F. JACQUELINE. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **2**, 345–357, April, 1957. 7 figs., bibliography.

The serum of 45 patients presenting with various arthritic manifestations of gout has been analysed by zone electrophoresis for proteins, glycoproteins and lipoproteins. Serial estimations were performed in 5 patients, 4 of whom had suffered exacerbations of the gout.

The serum of a gouty subject free of symptoms shows a slight diminution of the α_2 globulin and more pronounced of the corresponding glycoprotein and increase of β globulin and, most strikingly, of the corresponding glyco- and lipo-proteins. Alterations in γ lipoproteins are related to the severity of the disease and even more to the diet. The onset of a relapse is heralded by a fall in albumin and α_2 glycoproteins and an increase of β and γ lipoproteins.

The usual concomitants of inflammatory reaction (increased α_1 and γ glycoprotein) are found but rather late in relation to the appearance of the clinical signs and their return to the previous levels is rapid.

Alterations in the differential protein pattern or the sedimentation rate are marked only in severe exacerbations, suggesting a diminished ability of the body to react to the stimuli. The action of phenylbutazone, benemide [probenecid] and colchicine on these changes has been studied.—[Authors' summary (translated by A. M. Joekes).]

ACUTE RHEUMATISM

954. **Schönlein–Henoch Purpura. Evidence for a Group A β-Haemolytic Streptococcal Aetiology**
E. G. L. BYWATERS, I. ISDALE, and J. J. KEMPTON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **26**, 161–175, April, 1957. 7 figs., 18 refs.

This paper reports studies carried out at the Canadian Red Cross Memorial Hospital, Taplow, the Postgraduate Medical School of London, and the Royal Berkshire Hospital, Reading, on 52 patients (28 at Taplow and 24 at Reading) with Schönlein–Henoch purpura. The maximum incidence was between the ages of 10 and 12 years, only 7 of the 52 being over 12, and the sexes were equally affected. The onset in the majority of cases occurred between October and February. Four of the 52 patients had a second attack within one year of the first and one had 3 attacks. In all, 57 attacks were witnessed.

The characteristic rash, which starts as a pink maculopapule and within a few hours flattens and becomes dull red and later purple, finally fading after 3 or 4 days, was observed in all but one attack. Joint pain and swelling occurred in 38 attacks, abdominal manifestations (colicky pain) in 33, and melaena in 10, while one patient on 2 occasions developed an intussusception. Haematuria occurred in 23 attacks and localized patches of oedema were seen in 23 patients. Treatment seemed to have little effect and there was rapid and complete recovery except in about 10% of cases, in which proteinuria and haematuria persisted.

Although there was a history of a preceding infection of the upper respiratory tract in 41 attacks, in only 7 out of 30 cases were Group-A β-haemolytic streptococci isolated from the nasopharynx within a week of admis-

sion to hospital, and raised antistreptolysin-O titres were found in only 7 out of 19 cases. This is in marked contrast to a series of 107 cases of rheumatic fever examined during the same period, in which the incidence of a raised antistreptolysin-O titre was 76%. Thus despite the close clinical and pathological similarity between Schönlein–Henoch purpura, rheumatic fever, and acute nephritis, there is no clear evidence that the former invariably follows infection with Group-A β-haemolytic streptococci. *C. Bruce Perry*

955. **Social and Environmental Factors in the Aetiology of Rheumatic Fever**

P. E. GRAVE. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 602–608, May 4, 1957. 17 refs.

Certain aspects of the physical environment, the financial status of the family and the emotional climate of the home life of 120 children suffering from rheumatic fever were investigated. Similar inquiries were attempted for 100 children not suffering from rheumatic fever who were in the same age group and also came from the same socio-economic group; these children constituted the control group. A number of factors occurred more frequently in the families with children with rheumatic fever, and for some of these the differences were statistically significant compared with the control group. The number of families involved were, for some of these conditions, too few to justify their being considered as directly associated with the aetiology of rheumatic fever.

Overcrowding occurred in 31% of families with children with rheumatic fever, compared with 19% of controls. Of children with rheumatic fever 26% were living in damp houses, compared with 13% of controls. In 56% of the families with children with rheumatic fever income was judged to be marginal or inadequate, compared with 34% of the controls; in addition, 42% of the mothers of the former group compared with 13% of the controls were rated poor managers. Of mothers of children with rheumatic fever, 21% were judged to have a low maternal efficiency, compared with 5% of mothers of the control group. Once again it is considered that the total number of families involved is too small to justify a claim that low maternal efficiency is of itself a factor in the aetiology of rheumatic fever. Of families with children with rheumatic fever 66%, and 57% of families in the control group, were considered neither to initiate nor to avoid social activities outside the family. Of families in the control group 47% went out together regularly, compared with 29% of families with children with rheumatic fever. Of mothers with children with rheumatic fever, 61·5% were judged to be inadequate in their relationship with their child who had rheumatic fever; this figure contrasted with 28% of the controls. More than 50% of children in both groups came from the outer residential suburbs.

The observations in six areas—namely, housing, crowding, dampness, income, maternal efficiency, and mother–child relationship—were compounded for both groups. This analysis showed a high incidence of families with children with rheumatic fever to be inadequate in four, five and six areas compared with the controls, the three most commonly recurring factors being income, maternal efficiency and mother–child relationship. Other areas investigated were the parents' health, the routine of the household, undue desire for social advancement, separations from the mother, conjugal relationships, the attitude of fathers, the influence of grandparents, and the child in school. In the main the effects of these influences upon the children of both groups were similar, being in the direction of assisting the child's growth and development. In none of the areas investigated was the difference between the families with children with rheumatic fever and the control group sufficiently pronounced to justify a cause and effect relationship in the aetiology of rheumatic fever. However, the study did reveal the poor quality of family life in a significant number of families with children with rheumatic fever.—[Author's summary.]

956. **Plasma Fibrinogen in Rheumatic Fever**

J. REID and D. H. SPROULL. *British Medical Journal* [*Brit. med. J.*] **1**, 1089–1090, May 11, 1957. 2 figs., 3 refs.

The authors have determined the plasma fibrinogen concentration, as a possible measure of rheumatic activity, in 33 patients between the ages of 10 and 46 with febrile migratory polyarthritis diagnosed as rheumatic fever who were treated with aspirin at the Clinical Chemotherapeutic Research Unit of the Medical Research Council, Western Infirmary, Glasgow. The blood salicylate levels were maintained between 30 and 45 mg. per 100 ml., as determined by Trinder's method. The concentration of fibrinogen in the plasma was estimated gravimetrically at 0, 4, 7, 14, and 21 days and on discharge. It fell regularly and consistently, in contrast to Ernstene's findings (*Amer. J. med. Sci.*, 1930, **180**, 12). The authors attribute this fall to the effect of the salicylate [although no control series was studied]. When aspirin was temporarily discontinued the plasma fibrinogen level rose in 6 of the patients, only to fall again when a second course was given. [There is no mention of the erythrocyte sedimentation rate.]

The authors conclude that the results provide definite evidence that salicylate does more than relieve symptoms.

E. G. L. Bywaters

957. **Incidence of Rheumatic Fever in Relation to Immunologic Reactivity**

V. REJHOLEC. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 23–30, March, 1957. 2 figs., 12 refs.

Immunology tests were carried out at the Research Institute of Rheumatic Diseases, Prague, on 998 healthy male adolescents aged 15 to 16 years, subjects with a history of rheumatic fever or with clinical evidence of rheumatism being excluded. Each subject was given a subcutaneous injection of *Brucella abortus* bacterine, and 14 days later blood samples were taken from the cubital vein for estimation of the titres of agglutinins and incomplete antibody. Over a period of 9 months the subjects were under observation for clinical signs of rheumatic fever and sore throat; when sore throat developed the erythrocyte sedimentation rate (E.S.R.) was determined. The results were correlated with the

results of serological tests performed at the start of the investigation.

Rheumatic fever developed in 12 cases, and at first the antibody response was good; later on, however, some patients showed a less distinct change in the reactivity titre. When sore throat developed the E.S.R. was much higher in patients with a high antibody titre than in those with a low titre, the difference being more marked when the E.S.R. was determined after 2 hours than after one hour.

It is suggested that immunological grading might be of value in the detection of potential cases of rheumatism among the general population. On the other hand, since individual reactions vary and since it would be necessary to repeat the tests once a year, it is doubtful whether any public health authority would possess the facilities necessary for carrying out this form of investition. *A. Garland*

958. **Prevention of Recurrences of Rheumatic Fever**
E. G. L. Bywaters, K. Hallidie-Smith, and G. T. Thomas. *British Medical Journal* [*Brit. med. J.*] **1**, 1234–1235, May 25, 1957. 11 refs.

As continuous chemoprophylaxis with oral sulphonamides or penicillin has been found to be very effective against recurrences of rheumatic fever the authors consider that one of these drugs should be given as a routine to all patients convalescent from this disease. At the Canadian Red Cross Memorial Hospital, Taplow, Bucks, such routine prophylaxis has been in use since 1951, and all patients are given a supply of one of these drugs on discharge. The aim is to continue with this prophylaxis regularly until the patient reaches 20 years of age. Nevertheless, after the patient returns home this measure is frequently abandoned either because of parental apathy or because of the opposition of the general practitioner on medical or financial grounds or through ignorance. An examination of the reasons for medical opposition shows that most of them have some degree of validity, but it is suggested that the advantages of routine prophylaxis far outweigh its occasional possible disadvantages, which are avoidable. It is considered a matter for regret that relatively few hospitals in Great Britain practise such routine prophylaxis.

John Lorber

959. **Rheumatic Fever: Prevention of Recurrence with Penicillin Given Orally**
B. Dowd and H. Walsh. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 598–602, May 4, 1957. 2 figs., 20 refs.

Of 252 young patients admitted to the Royal Alexandra Hospital for Children, Sydney, in the period 1951–6 with a diagnosis of rheumatic fever or chorea, 86 were given penicillin orally as a prophylactic, the remaining 166 children serving as controls, of whom 71 received a course of sulphadiazine (0·5 g. twice daily for varying periods). For purposes of comparison the whole series of patients was divided into four groups according to the number of attacks they had undergone; attacks occurring within 3 months of the previous one were considered as relapses and not as recurrences. Penicillin was administered as soon as the diagnosis was definite, being given intramuscularly initially and then orally in the form of tablets containing 100,000 units of benzylpenicillin three times a day half an hour before meals. Administration was continued for 3 to 52 months (average 22 months) and the children in both groups were periodically reviewed.

There were 6 deaths in the series, all from rheumatic carditis and all in the control group (one after the first attack, 4 after the second, and one after the third). In the penicillin-treated groups there were 3 recurrences, whereas 10 recurrences developed in the patients given sulphadiazine and 70 in those receiving no form of drug prophylaxis (61 representing a second attack and 9 a third). Of 4 children in the treated group who subsequently stopped taking penicillin, 2 later suffered a recurrence, while of 4 children receiving penicillin who were found at some stage to have Lancefield Group-A β-haemolytic streptococci in their throat, none developed a recurrence. It is suggested that these cases may indicate that a higher dose of penicillin is required for prophylaxis. The recurrence rate after the first attack in children given no prophylaxis conformed to the natural history of the disease, a second attack occurring in nearly 70% within 5 years, with a peak incidence in the second year.

In view of the significant reduction in recurrences in patients receiving penicillin it is suggested that this treatment should be given prophylactically throughout childhood and adolescence, and probably even longer, to all children developing an attack of rheumatic fever or solitary chorea. *M. Kendal*

960. **Electrophoretic Studies of the Changes in the Serum Proteins with Rheumatic Chorea.** (Электрофоретическое исследование белков сыворотки крови в динамике у больных малой хореей)
L. T. Anisimova. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikiat.*] **57**, 49–52, No. 1, 1957. 1 fig., 10 refs.

The diagnosis of rheumatic (Sydenham's) chorea from choreiform syndromes of different aetiology is often difficult. At the First Moscow Medical Institute the author carried out investigations of the serum albumin and globulin (α_1, α_2, β, and γ) fractions in 48 children in an attempt to establish diagnostic and prognostic features. There were 30 patients with chorea, 3 with hyperkinesis and tics of rheumatic aetiology, 5 with choreic manifestations of other aetiology, and 10 healthy children as controls. Their ages ranged from 6 to 16 years.

Micro-electrophoresis on filter paper was carried out by a modification of Flynn and Mazo's method, with quantitative analysis. It was found that in the cases of chorea, as in other rheumatic cases, a dysproteinaemia regularly occurred, this taking the form of a reduction in the serum albumin and an increase in the α_2- and γ-globulin fractions. The relative increase in the α_2 globulins (10·6 to 13·4%) was greatest in those cases where the illness was the first attack, in contrast to

recurrent cases, in which hypergammaglobulinaemia was the rule (>26%). No significant changes in the α_1-globulin fraction were found, and an increase in the β-globulin fraction (16 to 17·2%) was observed only in 3 severe cases of chorea with toxaemia. Clinical recovery was not always accompanied by a return to normal of the serum protein picture, although the erythrocyte sedimentation rate fell, and a persistently raised α_2-globulin level was found in cases in which there was a subsequent relapse of chorea or the development of other rheumatic lesions. The increase in the γ-globulin fraction normally persisted longer (2 months) than that in the α_2 fraction, and an unduly rapid fall or low original level was found to be a bad prognostic sign.

No changes in the serum protein levels were observed in cases of non-rheumatic chorea, and the author considers the investigation to be of value both in the differential diagnosis of doubtful cases and as an aid in prognosis. *Alexander Duddington*

CHRONIC RHEUMATISM

961. **Steroid Pseudorheumatism**
J. Rotstein and R. A. Good. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 545–555, April, 1957. 1 fig., 20 refs.

The authors describe 5 cases in which patients receiving long-term steroid therapy for rheumatoid arthritis developed symptoms of "steroid pseudorheumatism" [which is the same as the hypercortisonism described by Slocumb *et al.* (*Ann. intern. Med.*, 1957, **46**, 86; *Abstracts of World Medicine*, 1957, **22**, 50)]. This syndrome manifests itself in periods of restlessness, asthenia, pains in the muscles, bones, joints, and tendons, and memory defect. The condition can be distinguished from rheumatoid arthritis by the absence of signs of articular inflammation and should be treated by gradual withdrawal of hormone therapy. *Oswald Savage*

962. **Plasma Proteins and Cryoglobulins in Anarthritic Rheumatoid Disease**
L. Bagratuni. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 104–110, March, 1957. 4 figs., 27 refs.

The syndrome of "anarthritic" rheumatoid disease has been described previously by the author (*Ann. rheum. Dis.*, 1953, **12**, 98; *Abstracts of World Medicine*, 1954, **15**, 65). This paper from the Radcliffe Infirmary, Oxford, describes the detailed chemical and electrophoretic analysis of the plasma proteins in 12 cases of this syndrome, 2 in males and 10 in females. The main changes noted were a reduction in level of the albumin fraction and a rise in that of the α_1 and α_2 globulins and of the fibrinogen. The β-globulin level was slightly increased. In 3 cases the presence of cryoglobulin was noted. In 2 cases there was a double β-globulin band, and in one of these the faster component corresponded to the cryoglobulin, which gelled at room temperature. Two of the cases with cryoglobulin had raised γ-globulin levels, as did one other case. The high plasma fibrinogen content and altered albumin:globulin ratio are thought to account for the considerable rise in erythrocyte sedimentation rate which is a feature of the syndrome.

An extensive discussion, with numerous references to the literature, provides a useful review of the changes in the pattern of the individual plasma protein fractions in the collagen diseases as a whole, the essential features of which are a fall in the albumin level and a rise in those of the α_1 and α_2 globulins and fibrinogen. The presence of these characteristic features is considered to provide evidence that this syndrome is a rheumatoid disease process of an anarthritic type. The good prognosis is in part due to the lack of extensive tissue destruction, which is reflected in the generally normal γ-globulin level. *Harry Coke*

963. **The Use of *alpha*-Chymotrypsin Applied Locally in Certain Rheumatic Conditions.** (Emploi de l'alpha chimotrypsine en application locale dans quelques processus rhumatismaux)
L. S. Sola, F. G. Valdecasas, P. P. Muset, and P. Barcelo. *Thérapie* [*Thérapie*] **12**, 194–199, 1957.

The pancreatic enzyme trypsin is said to have an anti-inflammatory action. From the University of Barcelona the results are reported of the treatment of scapulo-humeral periarthritis by periarticular injections of a similar proteolytic ferment, α-chymotrypsin, which has the advantage that it can be used in aqueous solution and causes far less local pain than an oily suspension of trypsin. In the 14 patients treated, 10 with acute or subacute and 4 with a chronic condition, the periarticular tissues were infiltrated with 5 mg. of α-chymotrypsin dissolved in 10 ml. of sterile normal saline, treatment being given on alternate days for 2 weeks, and then less frequently according to the degree of improvement.

The results are considered to be superior to those of any other treatment in current use. The first injection brought prompt relief of pain in most of the acute cases, and the range of movement at the shoulder quickly increased. Almost complete cure, with only a slight painless limitation of rotation remaining, was achieved with from 11 to 19 injections. Remedial exercises were also employed. *Kenneth Stone*

964. **Proposed Diagnostic Criteria for Rheumatoid Arthritis. Report of a Study Conducted by a Committee of the American Rheumatism Association**
M. W. Ropes, G. A. Bennett, S. Cobb, R. Jacox, and R. A. Jessar. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 118–125, March, 1957. 6 refs.

The authors describe a study carried out under the auspices of a Committee of the American Rheumatism Association and designed to work out a set of diagnostic criteria for rheumatoid arthritis in three categories, namely, definite, probable, and possible. The criteria were based mainly on information supplied by a group of physicians dealing with rheumatism in the United States and Canada, each of whom was asked to supply data concerning 5 recent cases of definite rheumatoid arthritis, 5 probable cases, and 5 cases "with no evidence

of rheumatoid arthritis". A total of 332 suitable case reports from 19 centres were received.

Analysing the data the Committee gave mathematical expression to the value of each criterion in diagnosis. From the results of their study they suggest 11 criteria for the diagnosis of "definite" rheumatoid arthritis, of which six are clinical signs and the other five radiological and laboratory findings. They also present a list of 19 findings or conditions, such as gout, lupus erythematosus, periarteritis nodosa, scleroderma, and others, the presence of any one of which will exclude a patient from the categories of definite, probable, or possible rheumatoid arthritis. [The value of the Committee's work will become apparent only if workers in this field read the original paper and adopt the criteria suggested. As the authors point out, rheumatoid arthritis is a disease in which the cause is unknown and the limits undefined. The use of the diagnostic criteria described would make it quite certain that the disease being described was, in fact, rheumatoid arthritis.]

William Hughes

965. **The Serological Diagnosis of Rheumatoid Arthritis.** (Zur serologischen Diagnostik der primär chronischen Polyarthritis)
J. LAVIČKA and V. ZAVÁZAL. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **16**, 112–116, April, 1957. 7 refs.

At the Institute of Microbiology, Pilsen, Czechoslovakia, the antistreptohyaluronidase and the sheep-erythrocyte agglutination tests (Heller's modification) were performed on the sera of 145 patients with rheumatoid arthritis and 30 patients with ankylosing spondylitis. The majority of the patients were actively ill. In the rheumatoid arthritis group the antistreptohyaluronidase level was raised in 15% of patients, but did not approach the levels customarily found in rheumatic fever. The sheep-cell agglutination reaction was positive in 81%. Statistically there was no positive correlation between the two tests. In practice the results of these two tests were found to be useful in differentiating atypical rheumatic fever from early rheumatoid arthritis.

Of the patients with ankylosing spondylitis, negative results in both tests were obtained in two-thirds, while in the remaining one-third the reaction was positive in one or both tests. In these patients the antistreptohyaluronidase titre was only slightly raised in those giving a positive reaction, a finding similar to that in the rheumatoid arthritis group and unlike the findings in patients with rheumatic fever. *G. W. Csonka*

966. **Augmenting Effect of Rheumatoid Sera in a Streptococcal Haemagglutination Test**
N. R. LING and H. J. GIBSON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 111–117, March, 1957. 2 figs., 24 refs.

When human Group-O erythrocytes, treated with the products of growth of Gram-positive organisms, are sensitized with an antibody-like principle present in approximately 18% of normal and pathological human sera, they are agglutinated by sera from cases of rheumatoid arthritis in a way which closely parallels the Rose–Waaler activity of the same sera. The titre of human sera against erythrocytes coated with the polysaccharide produced by Gram-positive organisms is a measure, not of antibody alone, but of antibody plus augmenting factor. It can be shown that the augmenting factor and sensitizing antibody may coexist in the same serum and react with human Group-O Rh-negative cells coated with polysaccharide from Gram-positive cocci. Some properties of the agglutinin augmenting factor are described and the significance of the results discussed. —[Authors' summary.]

967. **The Latex Fixation Test in Rheumatoid Arthritis**
J. W. THOMAS, H. S. ROBINSON, J. P. GOFTON, M. STUCKEY, and R. LAMONT-HAVERS. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 621–623, April 15, 1957. 3 refs.

The differential sheep-cell agglutination test of Rose and Waaler is now well known as an aid to the diagnosis of rheumatoid arthritis; an important part of this test appears to be the reaction between the gamma globulin coating the sheep erythrocytes and a factor (the R factor) in the serum of the rheumatoid patient. Recently, however, Singer and Plotz (*Amer. J. Med.*, 1956, **21**, 888; *Abstracts of World Medicine*, 1957, **22**, 50) described a modification of this test in which, instead of sheep cells, polysterene latex particles of uniform size (0·814 μ) are used.

The present authors, at the British Columbia Medical Research Institute, Vancouver, have subjected the sera of 105 patients with rheumatoid arthritis to this modified test and to the standard Rose–Waaler test. The latex test gave a positive result in 76 cases and the Rose–Waaler test in 58. In a further 81 cases of other rheumatic or collagen diseases no positive results were obtained with the standard test, but in one case of osteoarthritis the latex test gave a positive reaction. The authors consider that the latex fixation test shows a degree of specificity comparable with the best of the various modifications of the sheep-cell test, and moreover the materials required can be more easily obtained and stored. *B. E. W. Mace*

968. **Clinical and Radiological Studies of the Diencephalo-hypophysial Region in Rheumatoid Arthritis.** (Rilievi clinico-radiologici della regione diencefaloipofisaria nell'artrite reumatoide)
D. RIZZI and A. CAVALLO. *Reumatismo* [*Reumatismo*] **9**, 114–120, March–April, 1957. 5 figs., 20 refs.

The authors, working at the University of Bari, have estimated the area of the sella turcica in 31 patients (13 males and 18 females) suffering from rheumatoid arthritis, the area being determined from a study of lateral radiographs. The normal area was taken to be 95 sq. mm. in the male and 90 sq. mm. in the female. In 24 cases (about 70%) the area was reduced. The smallest area recorded was 33 sq. mm. a in 50-year-old woman. Abnormalities in the clinoid processes were noted in 10 of the patients. The detailed results are tabulated.

The authors consider that the clinical features suggest a dysfunction of the " diencephalo-hypophysial system ", and point out that in 4 cases there was hyperthyroidism, in 2 signs of *forme fruste* hypoadrenalism, and in one clinical acromegaly. The various theories of the aetiology and pathogenesis of rheumatoid arthritis are discussed, the role of the pituitary gland being emphasized. The authors claim that there is a frequent association between reduction of the area of the sella turcica and unbalanced pituitary function in rheumatoid arthritis. *David Friedberg*

969. **Phenylbutazone in Active Periods of Rheumatoid Arthritis. A Methodological and Controlled Clinical Trial.** [In English]
K. E. FJELLSTRÖM, L. GOLDBERG, G. LINDGREN, and F. NILSSON. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, Suppl. 320, 1–49, 1957. 14 figs., bibliography.

970. **Peripheral Vascular Obstruction in Rheumatoid Arthritis and Its Relationship to Other Vascular Lesions**
F. G. L. BYWATERS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 84–103, March, 1957. 29 figs., 39 refs.

From the Canadian Red Cross Memorial Hospital, Taplow, Bucks, and the Postgraduate Medical School of London the author describes in detail 10 cases of peripheral vascular obstruction in patients with rheumatoid arthritis. The condition was fatal in 2 cases, in one of which there were extensive visceral lesions; in the remaining 8 cases the digital arteries only were involved.

The first fatal case was originally believed to be one of disseminated lupus erythematosus, but detailed histological examination of the tissues post mortem ruled this out. The patient, a woman aged 28, developed signs of rheumatoid arthritis and a rash suggestive of lupus erythematosus in 1944. After about 3 years, during which period many bizarre symptoms such as Raynaud's disease and recurrent blisters on the fingers were recorded, the patient developed gangrene of the hands and feet and died. The outstanding histological finding at necropsy was widespread obliterative endarteritis with minimal periarteritis. The second fatal case occurred in a 37-year-old man who had suffered from severe and progressive rheumatoid arthritis for some 12 years, for which he was treated with cortisone without obvious benefit. Gangrene eventually developed and progressed. At post-mortem examination there were signs of gross amyloid disease in the spleen, kidneys, and adrenal glands, and proliferative endarteritis involving the peripheral and visceral arteries.

In the remaining 8 cases the most common lesions were thromboses in the nail-folds or pulp of the finger leading to necrosis, giving rise to pigmented scars and atrophy of the pulp; these appearances are illustrated in the text. L.E. cells were found in the blood in 3 cases but repeated examinations did not disclose their presence in the others.

In discussing the differential diagnosis in these cases in detail the author rules out Buerger's disease and polyarteritis nodosa, and regards the vascular lesions as part of malignant rheumatoid arthritis. He adds: " it is not felt that cortisone played any important part since only 3 of the 10 [patients] had had such preceding treatment ". *William Hughes*

971. **Quantitation of the Activity of Rheumatoid Arthritis. 6. Correlation of Systemic and Joint Findings**
J. LANSBURY and S. M. FREE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 375–378, April, 1957. 3 figs., 3 refs.

This is the sixth in a series of articles from Temple University School of Medicine, Philadelphia, in which the senior author has endeavoured to establish an acceptable clinical index of activity in rheumatoid arthritis. In two previous papers (*Amer. J. med. Sci.*, 1956, **232**, 150 and 300) he described what he terms the " articular index " and the " systemic index ". In the present paper is recorded a correlation between these two which is considered to support the previous claim that the systemic index measures the activity of the disease with reasonable accuracy. This index is based on such general manifestations as can be objectively measured—stiffness, fatigue, strength of grip, erythrocyte sedimentation rate, and aspirin requirements. The claim for its reliability has hitherto rested, however, upon indirect evidence and " clinical impression ".

It is now reported that simultaneous paired determinations of the systemic and articular indices in 80 unselected cases of active rheumatoid arthritis showed a striking correlation between the two. As the articular index is based upon the simplest and most reliable type of clinical observation of the degree of joint function it is considered that this correlation indicates a high degree of reliability. The authors recommend use of their articular and systemic indices as rapid and reasonably accurate methods for recording the activity of, and summarizing the joint findings in, rheumatoid arthritis.
W. S. C. Copeman

972. **The Behaviour of Urinary Glycoproteins in Rheumatic and Other Diseases.** (Sul comportamento dei glicoprotidi urinari nelle malattie reumatiche e in alcune altre condizioni morbose)
E. BONOMO and P. CERRETELLI. *Reumatismo* [*Reumatismo*] **9**, 98–113, March–April, 1957 3 figs., bibliography.

In a study carried out at the Rheumatological Centre, University of Milan, the daily urinary excretion of acid mucopolysaccharides was determined in 12 normal subjects, 17 patients with rheumatic diseases, and 11 others with various non-rheumatic diseases. The urinary mucoprotein excretion was also estimated in 5 normal and 7 rheumatic subjects and the glycoprotein excretion in 10 normal subjects, 9 rheumatic patients, and 16 with other diseases.

It was found that the excretion of acid mucopolysaccharides was increased in both the rheumatic patients and those with non-rheumatic diseases, the mean value being 5·5 mg. of glycuronic acid per 24 hours, compared with 3·7 mg. in normal subjects. Excretion of glycoprotein (precipitated by phosphotungstic acid) showed a

similar increase, the patients having a mean of 16·0 mg. of glucosamine hydrochloride per 24 hours compared with 7·0 mg. in the controls. The differences in both these values are statistically highly significant ($P<0.001$). There was no significant difference in relation to sex or between patients with rheumatic disease and those with non-rheumatic disease. On the other hand there was no difference in the urinary excretion of mucoproteins between the normal subjects and the patients with and without rheumatic disease.

The authors present a graph showing the serum mucoprotein levels for each patient plotted against urinary glycoprotein excretion. The result is a straight line, the correlation coefficient being 0·827. There is a full discussion of the literature on this subject.

David Friedberg

973. **Long-term Results in Early Cases of Rheumatoid Arthritis Treated with Either Cortisone or Aspirin**

MEDICAL RESEARCH COUNCIL/NUFFIELD FOUNDATION JOINT COMMITTEE ON CORTISONE, ACTH, and OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES. *British Medical Journal* [*Brit. med. J.*] **1**, 847–850, April 13, 1957. 6 refs.

This is the third report of a comparative study of the use of cortisone and aspirin in the management of 61 cases of rheumatoid arthritis. When the investigation started in 1951 a criterion for treatment was a history of rheumatoid arthritis of only 3 to 9 months' duration. The patients were aged 17 to 59 years, and in each case 4 joints or more were affected, with bilateral disease of the hands, wrists, ankles, or feet. In the majority of cases the sheep-cell agglutination test yielded a positive result at least once. [For the previous reports see *Brit. med. J.*, 1954, **1**, 1223, and 1955, **2**, 695; *Abstracts of World Medicine*, 1954, **16**, 405, and 1956, **19**, 229.]

The therapeutic trial in its original form was discontinued after the second year, and the present report reviews the condition of the 53 patients remaining under observation 3 to 4 years later. At that stage the mean daily dosages of cortisone and aspirin in those still taking these drugs were 66 mg. and 3·5 g. respectively. Cortisone therapy had been discontinued in 4 cases owing to the advent of side-effects such as dizziness, hypertension, dyspepsia, and moon-face. The results of treatment were evaluated by assessment of the general functional capacity, the number of remissions, and the average haemoglobin level and erythrocyte sedimentation rate. Changes in porosis and erosion were estimated by studying the radiological appearances of the hands and feet. With regard to the outcome of treatment, there appeared to be no significant advantage in employing cortisone therapy; in fact, some patients preferred aspirin. Administration of these drugs brought about remission in 25% of cases, but the disease remained very active in a similar proportion.

A. Garland

974. **Corticosteroid Metabolism and Rheumatoid Arthritis**

H. F. WEST. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 173–182, June, 1957. Bibliography.

975. **Placebos in the Treatment of Rheumatoid Arthritis and Other Rheumatic Conditions**

E. F. TRAUT and E. W. PASSARELLI. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 18–22, March, 1957. 9 refs.

The authors, working at Cook County Hospital, Chicago, with patients who had all been previously exposed to many different agents for the treatment of rheumatoid arthritis, report the result of giving placebo tablets, each containing 0·2 g. of lactose, which were taken daily after meals for as long as the patient continued to report improvement. If no improvement was reported the lactose was given by hypodermic injection, and if this too failed the patient was treated with one of the current antirheumatic drugs. The series consisted of 88 out-patients, of whom 51 received the treatment for 4 weeks or less. Of the latter, 13 (25%) reported moderate (9) or marked (4) improvement. Of the remaining 37 patients treated for up to 18 months, 17 reported moderate and 14 marked improvement. The longer the tablets were taken, the higher the percentage of patients reporting improvement [but this appears to be due to the fact that only those experiencing some benefit asked for the therapy to be continued]. The improvement was largely subjective, no radiological improvement being observed in any of the cases. Lactose given by injection relieved 25 (64%) out of the 39 who were resistant to the tablets, this relief occurring just as frequently in severe as in mild cases. Some patients claimed that injections in the vicinity of painful joints were more effective than those at a distance. The authors comment that the proportion of rheumatoid arthritic patients benefited by a placebo is very much the same as that claimed for any current form of antirheumatic treatment, including salicylates and even cortisone.

William Hughes

976. **Rheumatoid Aortitis with Aortic Regurgitation. An Unusual Manifestation of Rheumatoid Arthritis (Including Spondylitis)**

W. S. CLARK, J. P. KULKA, and W. BAUER. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 580–592, April, 1957. 11 figs., 27 refs.

The authors have studied 22 cases in which aortitis and aortic endocarditis were associated with rheumatoid spondylitis or rheumatoid arthritis observed over a period of 20 years at the Massachusetts General Hospital, Boston. The patients had signs of aortic regurgitation without evidence of mitral stenosis; those suspected of having had syphilis or preceding attacks of rheumatic fever were not included in the study.

Serological tests for syphilis gave negative results. Three of the patients developed pericarditis, 8 angina pectoris, and 10 congestive cardiac failure. All but 6 of the 22 patients died, a cardiac lesion being the cause of death in 13 cases. Post-mortem examination was carried out on 9 patients. Secondary amyloidosis was present in 3 cases. The aortic valve rings were found to be dilated. The valve cusps showed varying degrees of fibrosis, with thickening and retraction; the cusps were usually separated rather than adherent, though a few

adhesions were seen. The aortitis was characterized grossly by discrete intimal plaques extending from the valve for about 2·5 cm. distally into the ascending aorta, the coronary ostia being distorted by these lesions in 2 cases. Microscopically, the intimal thickening was the result of subendothelial connective-tissue proliferation and increase in mucinous ground substance. Irregular focal destruction of the media associated with ingrowth of vascular granulation tissue was noted. There was also fibromuscular thickening of the vasa vasorum, with obliteration of the lumen in some instances. *C. E. Quin*

977. **Differential Diagnosis of Ankylosing Spondylitis**
J. SHARP. *British Medical Journal* [*Brit. med. J.*] **1**, 975–978, April 27, 1957. 4 figs., 31 refs.

Because of certain dangers in the deep *x*-ray treatment of ankylosing spondylitis it is important to establish the diagnosis of this disorder beyond doubt so as to avoid exposing any patient to risk unnecessarily. Among a series of 530 patients attending a special spondylitis clinic at Manchester Royal Infirmary the author has found that about one in five was not a genuine case of spondylitis ankylopoietica. These atypical cases all showed involvement of the sacro-iliac joints, but they also presented unusual clinical or radiological features suggestive of other diseases, such as rheumatoid arthritis, Reiter's disease, acute rheumatism, or psoriatic arthritis.

He has therefore studied the occurrence of spondylitis in the above conditions to see how far it was possible to establish an exact diagnosis. (1) In rheumatoid arthritis clinical involvement of the spine is uncommon, and although some radiological evidence of disease can be demonstrated in about 50% of these cases, the radiological changes differ in many respects from those of ankylosing spondylitis. Involvement of the cervical spine is more common; here the joint spaces are narrowed but there is absence of the characteristic "bambooing" of the spine seen in ankylosing spondylitis. (2) In rheumatic fever spinal lesions are rare, but 19 cases of such lesions were identified among 2,000 patients with acute rheumatism; all 19 patients had suffered repeated attacks of rheumatic fever and all had valvular lesions of the heart. The differential sheep-cell agglutination test was negative in all of the 16 cases tested. The sacro-iliac joints were involved in half these patients and the radiological appearances in many cases were indistinguishable from those in ankylosing spondylitis. However, the history of the disease, the ligamentous laxity, and the effusion into the peripheral joints all helped to clarify the diagnosis in difficult cases. (3) Of the 20 patients with Reiter's disease, 4 had developed severe restriction of spinal movements and some showed radiological involvement of the sacro-iliac joints. However, a history of dysentery or urethritis together with the occasional incidence of keratodermia or iritis were pointers to the correct diagnosis. (4) There was some spinal involvement in 11 out of 68 cases of rheumatoid arthritis complicated by psoriasis. But whereas extensive involvement of the peripheral joints was found in these cases, radiological involvement of the sacro-iliac joint was not a notable feature. There were also changes in other areas in the spine, but these were more suggestive of rheumatoid arthritis than of ankylosing spondylitis.

The author concludes by stressing that exact diagnosis is of great importance in these cases, since treatment by deep *x*-ray therapy may be of real benefit in cases of true ankylosing spondylitis, but is useless in the other conditions. *William Hughes*

COLLAGEN DISEASES

978. **Six Years' Survival in Severe Systemic Lupus Erythematosus. An Analysis of Twelve Cases**
J. R. HASERICK. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 706–714, May, 1957. 11 figs., 10 refs.

From the Cleveland Clinic Foundation, Cleveland, Ohio, are reported 12 cases (2 in males and 10 in females) of severe systemic lupus erythematosus in which the patients have lived 6 years or more after an acute episode from which they were not expected to recover. Summaries of the case histories are given and photographs illustrate selected cases. Four of the patients originally came under observation following the discovery of false positive results of serological tests for syphilis. All 12 patients except one received steroid therapy during the acute phases of the disease, but the most dramatic therapeutic response was seen in 2 cases where steroids were combined with nitrogen mustard, although in one of these cases a severe leucopenia developed. Among adjuvant methods of treatment employed were *x*-irradiation of the ovaries (in 3 cases) and administration of antimalarial drugs. Such preparations were considered particularly useful as agents against photosensitivity and may have some value in reducing the dosage of steroids required for control. The author considers that steroid treatment is specifically indicated for acute episodes until a remission occurs, and that it may also be used during pregnancy or during surgical procedures to guard against possible untoward effects due to instability of the disease. Although it is recommended that pregnancy be avoided, it should be permitted to go to term when it does occur. During remissions in the cases reported L.E. tests, previously positive, became negative and serum protein electrophoretic patterns changed towards normal; even so it is suggested that although stable remissions may be obtainable, it is doubtful whether true "cures" occur.
Benjamin Schwartz

979. **The Lupus Erythematosus Syndrome: the Relationship of Discoid (Cutaneous) Lupus Erythematosus to Systemic (Disseminated) Lupus Erythematosus**
A. J. REICHES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 678–684, April, 1957. 19 refs.

The author has sought to elucidate the relationship between cutaneous and disseminated lupus erythematosus by means of a questionary sent (1) to 1,200 Fellows of the American Academy of Dermatology, of whom 792 replied; and (2) to 135 "internists", 100 of whom replied. By this method [which has obvious

drawbacks] he has collected information about 353 cases of discoid lupus erythematosus known to have been followed by disseminated lupus erythematosus. Of the 353 cases, L.E. cells were found in 97. It also appeared that the chronic localized discoid form of the disease often was present for many years before the development of the disseminated form.

Case histories are appended of 3 patients who had had chronic discoid lupus erythematosus for 13, 10, and 6 years respectively, and who then developed the acute disseminated form of the disease. In all 3 cases L.E. cells were found together with leucopenia, thrombocytopenia, and reversal of the albumin:globulin ratio. Despite steroid therapy 2 of the 3 patients died shortly after the onset of disseminated lupus erythematosus.

J. N. Harris-Jones

980. **Systemic Lupus Erythematosus. A Report on Twelve Cases Treated with " Quinacrine " (" Atabrine ") and Chloroquine (" Aralen ")**

S. K. CONNER. *Annals of the Rheumatic Diseases* (*Ann. rheum. Dis.*] **16**, 76–81, March, 1957. 23 refs.

The 12 patients whose treatment is described in this report were regarded as having definite systemic lupus erythematosus, as shown by the demonstration of L.E. cells in the blood or bone marrow and by such signs as skin rash, serositis, oedema, purpura, ulceration of nodules and skin, and arthritis. Mepacrine (" atabrine ", " quinacrine ") was given in a dosage of 100 mg. 3 times a day, this being later reduced to once a day. (One patient received chloroquine instead.) Five of the patients received small amounts of ACTH (corticotrophin) or prednisone as well. Treatment was continued up to 32 months, and all patients are reported to have shown improvement, with a fall in the erythrocyte sedimentation rate in many cases. No serious complications resulted from the treatment. *K. C. Robinson*

981. **Clinical Features of Polyarteritis Nodosa with Lung Involvement**

G. A. ROSE. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **51**, 113–122, April, 1957. 4 figs., 25 refs.

This paper from St. Mary's Hospital, London, describes the pulmonary manifestations of polyarteritis nodosa, " since these are unfamiliar and often lead to errors in diagnosis ". It is based on a survey of 111 cases of polyarteritis nodosa undertaken for the Collagen Diseases and Hypersensitivity Panel of the Medical Research Council and previously reported by Rose and Spencer (*Quart. J. Med.*, 1957, **26**, 43; *Abstracts of World Medicine*, 1957, **22**, 133). The lungs were involved in one-third of these cases.

Three types of pulmonary involvement are recognized and designated respectively pneumonic, bronchitic, and asthmatic. Records of cases illustrating the 3 types are presented. Three cases of the pneumonic type are described. In each case extensive pulmonary disease, considered to be and treated as tuberculosis in 2 cases, preceded the onset of generalized symptoms, with the development of which the illness was recognized as polyarteritis nodosa. The bronchitic variety is typified by a case in a woman who presented with a productive cough and in whom radiological examination showed minimal diffuse pulmonary infiltration. An accompanying proteinuria suggested polyarteritis, and this was confirmed by muscle biopsy. Finally 2 cases are described in which periodic attacks of asthma dominated the clinical picture. Despite associated symptoms such as haemoptysis, haematuria, and subcutaneous nodules, the correct diagnosis was not reached in the first case (in a woman of 40) until material removed during a lobectomy for bronchostenosis was examined. Both lungs showed cystic changes, but the disease was controlled by administration of steroids. In the second case, in a boy of 16, the diagnosis was made only at necropsy following his sudden death 17 months after the onset of the illness.

There do not seem to be any specific radiological changes when the lungs are involved in polyarteritis nodosa, but the presence of diffuse miliary stippling and transient pulmonary infiltrates is regarded as suggestive, and cystic cavities of any variety may be seen. It appears that the pulmonary phase of polyarteritis nodosa may often precede generalized systemic spread of the disease, but it is not considered possible to make a diagnosis with any degree of certainty at this stage of the illness. *J. N. Harris-Jones*

982. **Pulmonary Lesions in Polyarteritis Nodosa**

H. SPENCER. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **51**, 123–130, April, 1957. 6 figs., 25 refs.

Five cases showing pathological evidence of pulmonary polyarteritis nodosa are reported from St. Thomas's Hospital, London. The first 2 cases were included in the 111 cases reviewed by Rose and Spencer and referred to in Abstract 981. Both were in middle-aged men who presented with respiratory symptoms together with evidence of extensive involvement of skin, retina, mucous membranes, and kidneys. Post-mortem studies revealed that, apart from widespread lesions of polyarteritis nodosa in most viscera, there were particularly striking changes in the lungs and upper respiratory tract. Ulceration extended from the tongue to and including the larynx. There were well-defined areas of consolidation with cavitation in the lungs and, microscopically, complete loss of lung tissue. The pulmonary vasculature adjacent to these areas of cavitation showed changes typical of polyarteritis nodosa. This association of pulmonary and upper respiratory granulomata has been previously referred to as Wegener's syndrome.

The remaining 3 patients had pulmonary hypertension, in one as a result of emphysema and in 2 associated with mitral stenosis. All 3 patients died, and in all 3 microscopy revealed evidence of an arteritis in the smaller pulmonary vessels. The author claims that he was able to distinguish these changes from those found commonly in pulmonary hypertension, and despite the absence of evidence of polyarteritis nodosa elsewhere, considers that these 3 cases are examples of pulmonary hypertensive polyarteritis. *J. N. Harris-Jones*

Neurology and Neurosurgery

983. **The Effect of Tolazoline Hydrochloride on Tic Douloureux**
E. W. POOLE. *Lancet* [*Lancet*] **1**, 805–806, April 20, 1957. 4 refs.

The results of treatment with tolazoline hydrochloride of 9 patients with tic douloureux, 2 of whom had disseminated sclerosis and one an acoustic neuroma, are reported from the United Oxford Hospitals. After a dose of 12·5 mg. of tolazoline by mouth to test for idiosyncrasy, graduated intravenous administration of up to 50 mg. in 10 to 15 minutes was the method preferred. Of the 8 cases so treated there was a dramatic cessation of attacks and inactivation of trigger areas, persisting for some hours in 6. One of the 2 patients who did not respond was later found to have an acoustic neuroma, while the other showed smaller peripheral vascular responses than usual. One patient with disseminated sclerosis was treated by the oral route (50 mg. thrice daily) for 3 months, and this resulted in a remission lasting for a year. The effect of tolazoline in suppressing the paroxysms of tic douloureux may be due to the relief of nerve ischaemia. *I. Ansell*

984. **Serum Lipids in Patients with Multiple Sclerosis**
B. GERSTL, W. E. DAVIS, J. K. SMITH, P. M. RAMORINO, and D. L. ORTH. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **27**, 315–320, March, 1957. 22 refs.

The levels of polyunsaturated fatty acids, total lipids, lipid phosphorus, and cholesterol were determined in the serums of 11 patients with MS in the "active," and in 9 patients in the "inactive" phase; serums from 8 patients with various nonmetabolic diseases were used as controls. The levels of dienoic acid in the serums of the patients with "inactive" MS were significantly higher than those in the other 2 groups. No significant differences were observed in the levels of the other lipids. —[Authors' summary.]

985. **The Amyotonia Congenita Syndrome**
J. N. WALTON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **50**, 301–308, May, 1957. 29 refs.

[This is an excellent review of the conditions which may cause the clinical syndrome of amyotonia congenita.] These fall into three groups: (1) infantile spinal muscular atrophy (Werdnig–Hoffman) in which the prognosis is bad; (2) symptomatic hypotonia, which may occur in progressive muscular dystrophy, in cerebral disorders such as mental defect and flaccid diplegia, and in metabolic conditions such as rickets and cretinism, and in which the prognosis depends on the underlying disease; and (3) benign congenital hypotonia. The author uses this last term to describe the cases in which there is severe hypotonia in infancy but in which progressive improvement occurs, although some residual muscle weakness may persist. He discusses the difficulties of accurate diagnosis in the case of hypotonic babies.
J. W. Aldren Turner

BRAIN AND MENINGES

986. **Developmental Abnormalities in the Region of the Foramen Magnum**
J. D. SPILLANE, C. PALLIS, and A. M. JONES. *Brain* [*Brain*] **80**, 11–48, March, 1957 (Part 1). 18 figs., bibliography.

It has been shown by Record and McKeown in a large series that the nervous system is one of the most common sites of malformation, the incidence of such anomalies being estimated at 0·6% of all notified births. Some malformations of the nervous system or of its bony envelope, the skull and spine, may give rise to no clinical symptoms until adult life is reached.

The skeletal anomalies discussed in this study, reported from the United Cardiff Hospitals, included fusion of cervical vertebrae, occipitalization of the atlas, atlanto-axial dislocation, and platybasilar impression, all in the region of the foramen magnum. It was based on 24 cases showing neurological signs in association with the above developmental anomalies seen in South Wales in the period 1947–56 and also on a full review of the literature. The radiological and clinical features are analysed critically, topics receiving special attention including the distinction between platybasia and basilar impression, the physical appearance of the patients, the clinical signs, and the pathogenesis of associated neural anomalies, for example, syringomyelia and downward displacement of the cerebellum. The classification of these syndromes is also considered. Operation was performed in 8 of these cases, but the authors observe that the diversity of the clinical picture and of the pathological findings at operation make it essential that each case be considered on its own merits. *L. Crome*

987. **Lesions of the Hypothalamic Region and Serum-protein Levels**
P. LOMAX. *Lancet* [*Lancet*] **1**, 904–907, May 4, 1957. 2 figs., 7 refs.

The effect of focal lesions of the brain on protein metabolism seems to have been inadequately investigated. The author, working at the Royal Infirmary, Manchester, has therefore determined the serum protein levels in 7 patients who had a primary lesion of the hypothalamic region, in 3 cases due to head injuries sustained in car crashes and in the 4 others to adjacent brain tumour. The results were compared with the findings in 44 control cases in which this particular region of the brain was not involved. In the patients there was a reversal of the albumin:globulin ratio in

the serum, in some cases the serum albumin level falling as low as 1·9 g. per 100 ml. while the serum globulin level rose to 5·2 g. per 100 ml.; these changes were independent of the dietary intake of protein.

Since in the 44 control cases there was no such change in the serum protein levels it is suggested that the hypothalamic structures in some way play a part in the modification of protein metabolism. It is believed that the first change to develop is a fall in the serum albumin level, and that this is closely followed by a rise in the serum globulin level. In patients recovering from the lesion the serum albumin level returned to normal before the globulin level fell. It is of interest to note that at all times the total serum protein level was normal, the fall in serum albumin being balanced by a rise in serum globulin level. In none of the 7 patients with disturbance of the serum protein pattern could any change in the serum electrolyte pattern or the level of blood urea be detected. The mechanisms by which these alterations are effected are obscure, but it is suggested that determination of the serum protein pattern may be of value in confirming that a lesion is affecting the hypothalamic region, and also possibly in assessing the first signs of recovery in certain cases of head injury before there is any real clinical improvement or alteration in the level of consciousness. *L. A. Liversedge*

988. **Structural Characteristics and Physiological Significance of Certain Parts of the Highest Levels of the Central Nervous System.** (Некоторые особенности структурных отделов центральной нервной системы и их физиологическое значение)
S. A. Sarkisov. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **57**, 15–22, No. 1, 1957.

[This is a comprehensive paper reviewing and correlating the results of neuro-anatomical and neurophysiological researches by various Soviet and other workers in the field of " higher nervous activity ".]

Writing from the Brain Institute, Moscow, the author describes the comparative anatomical studies which show the phylogenetic and individual differences in the gross and cyto-architectonic development of the various cortical analysers, and quotes recent experimental work on the relationship between certain hitherto obscure cortical areas with subcortical structures. For example, on the basis of these studies it is now possible to assert that one part of the insular area relates to the olfactory analyser and another to the cortical end of the speech-motor analyser.

Reference is made to the author's own work on the qualitative and quantitative differences in the stellate cells in the various layers and regions of the cortex, and he discusses the significance of these in the processes of retention and fixation. His own studies of the interneuronal connexions have shown that axo-dendritic contacts greatly preponderate over axo-somatic ones in the cerebral cortex, and the physiological functions of the cortex are discussed in relation to this finding and to the experimentally demonstrated changes in the dendrites that occur under the influence of neostigmine and other chemical agents. *Alexander Duddington*

989. **Thromboangiitis Obliterans Cerebri (Buerger's Disease). Diagnostic and Therapeutic Problems.** [In English]
T. Lehoczky. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **32**, 58–76, 1957. 3 figs., 20 refs.

The diagnosis and treatment of cerebral thromboangiitis obliterans, based on a total of 39 cases seen during the period 1942 to 1954, are discussed in this paper from the István Hospital, Budapest. The organic symptoms, which may resemble those of a brain tumour or of recurrent vascular occlusion, are at first of a transient nature and may be isolated or bilateral. The blood pressure, the erythrocyte sedimentation rate, the blood picture, urine, and cerebrospinal fluid are normal or only slightly abnormal. Ventricular dilatation with increased amounts of air in the subarachnoid space may be seen in the pneumoencephalogram, but there may be absence of filling on one side due to cerebral oedema. This cerebral oedema is more likely to be found in early cases than in advanced ones, where atrophy may occur and cause localized accumulations of air. Arteriography is not very valuable in diagnosis and, in the author's view, should only be used in the differential diagnosis of a tumour. The optic fundi are as a rule normal; hemianopia is rare as a focal symptom, while vitreous haemorrhages and choked disk are even rarer. Long-term observation of the patient is necessary if the diagnosis is to be firmly established. The aetiology is probably multiple, and at the same time largely dependent on hereditary or acquired allergic sensitivity. Clinical differentiation from cerebral arteriosclerosis and tumour may be difficult. Some forms of cortical atrophy, such as Pick's disease and Alzheimer's disease, may be simulated. Thrombus formation and recanalization play a part in the development of the clinical picture and the course of the disease.

The treatment of cerebral thromboangiitis obliterans by various [unconvincing] medical measures is discussed, as is surgical treatment by, for example, cervical sympathectomy and resection of affected portions of arteries [but no effective results of these procedures are recorded]. *J. MacD. Holmes*

990. **Anticoagulation Therapy in Cerebral Thrombosis and Embolism**
C. S. Ushiro and W. F. Schaller. *Neurology* [*Neurology*] **7**, 253–258, April, 1957. 3 figs., 18 refs.

At the Veterans Administration Hospital, Oakland, California, 24 selected patients admitted with cerebrovascular thrombosis, diagnosed mainly on the clinical findings and on the absence of erythrocytes in the cerebrospinal fluid, were treated with heparin and dicoumarol in doses such as to maintain the prothrombin time at about twice the control time, or between 10 and 20%. Anticoagulant therapy was discontinued if bleeding occurred as a complication. The object of the trial was to assess the ability of these drugs to prevent the extension of thrombo-embolism or cerebral infarction. A group of 39 similar patients served as controls, particularly in regard to degree of recovery, mortality,

and necropsy findings. Out-patient therapy was unsatisfactory, even with prothrombin estimations every 2 or 3 days, owing to variations in the prothrombin time [but this conclusion seems to be based on only one case].

Apart from stressing the danger of haemorrhage, the authors observe that complete occlusion of a basilar artery and thrombosis of the aorta, right iliac artery, femoral vein, internal carotid artery, pulmonary artery, and middle cerebral arteries all occurred at " effective " prothrombin levels. In addition, an extension of the thrombosis was not prevented in 2 cases. At the end of 18 months' follow-up there were 6 deaths in the study group (23%) and 6 (16%) in the control group. The necropsy findings are briefly noted. The authors conclude from their results that the dangers of anticoagulant therapy outweigh its theoretical value, pointing out that there was no difference in the incidence of complications and the course of the disease between the untreated and treated groups of patients.

[The conclusion drawn by these authors from their admittedly small series of cases should not interfere with further work on anticoagulant therapy in cerebral thrombosis. In the abstracter's experience more stable prothrombin levels might have been achieved with " dindevan " than with dicoumarol. The efficacy of anticoagulant treatment, even in coronary occlusion, is by no means settled, although its ability to reduce the incidence of venous thrombo-embolism in the legs seems certain. Long-term out-patient anticoagulant therapy is still in the testing stage.] *Fergus R. Ferguson*

991. **Aneurysms on the Anterior Cerebral Artery. Evaluation of Surgical and " Conservative " Treatments**
C. H. H. BAUMANN and P. C. BUCY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1448–1454, April 20, 1957. 3 figs., 13 refs.

The authors have reviewed the records of all patients with aneurysm of the anterior cerebral arterial system seen during a period of 10 years at the Chicago Wesley Memorial Hospital. These numbered 22, 18 being males and 4 females, aged between 33 and 56 years. All patients had suffered one or more subarachnoid haemorrhages. It was noted that prolonged unconsciousness, severe hemiparesis, retinal haemorrhages, and the presence of papilloedema indicated a poor prognosis.

Angiography was performed on 15 patients and in each case showed an aneurysm. In 3 cases there were multiple aneurysms. On an average angiography was performed 9·8 days after the last bleeding episode. The only complication was a contralateral seizure in one patient, which had no permanent sequelae. Of the 22 patients, 7 were treated conservatively, 3 had decompression with evacuation of haematoma, and one ligation of the common carotid artery. All but one of these 11 patients died. The remaining 11 patients were operated on. Clipping of the parent anterior cerebral artery was performed in 5 cases, clipping of the parent artery with packing of the aneurysm in 2 cases, and " trapping " of the aneurysm between clips in 4 cases. At follow-up at an average of 4 years after operation 7 of these 11 patients were well and had no residua, one had hemiplegia and aphasia (both of which were present before operation), one had died, and the fate of the remaining 2 was unknown.

On the basis of this study the authors conclude that cerebral angiography is an essential prerequisite to the proper treatment of bleeding intracranial aneurysms. While conservative treatment " is the most dangerous form of management of aneurysms of the anterior cerebral system ", clipping of one anterior cerebral artery may in most cases offer an effective alternative. However, exclusion of the aneurysm from the circulation is more desirable, but is also more hazardous.

Marcel Malden

992. **Subarachnoid Hemorrhage in Subacute Bacterial Endocarditis**
H. RAY and K. M. WAHAL. *Neurology* [*Neurology*] 7, 265–269, April, 1957. 6 figs., 12 refs.

This paper from Philadelphia General Hospital contributes 4 further examples to the published cases of subarachnoid bleeding in bacterial endocarditis—a relatively rare complication. All 4 terminated fatally and post-mortem examination revealed a mycotic aneurysmal lesion in 2 cases and an infected or necrotic " congenital " aneurysm in the other 2. Some of the features are rather unusual in subacute bacterial endocarditis, in that one patient also had purulent encephalitis and another showed destruction of the cusps of the mitral valve, foci of " metastatic nephritis ", an acute abscess near the mycotic aneurysm, and *Streptococcus pyogenes* in the blood. In a third case a septic clot was present, causing an arteritis [but no blood culture is recorded].

[Altogether the lesions described appear to have been unusually " septic " and the term " subacute " might well have been omitted in at least 2 of the cases in which the recorded length of illness was only 2 and 4 days respectively. Further, the part played by mycotic aneurysm in producing haemorrhage in 2 cases seems uncertain, since in one of these there was arterial occlusion with arteritic dilatation and in the other cerebral infarction, to which the bleeding may have been secondary, as no definite rupture of the aneurysmal dilatation is described. Other unfortunate omissions in this somewhat sketchy report are: no mention of the arterial blood pressure in the patient with coarctation of the aorta, and no accurate account of the duration of the illness in 3 cases. It would also appear that no therapy was given, since none is recorded. Finally the sizes of the aneurysms and the precise locations of the mycotic variety are not described, although this defect in the reports of other authors is the subject of comment.]

The authors point out that it should not be assumed that all aneurysms found in cases of bacterial endocarditis are mycotic in origin. (The term mycotic aneurysm was introduced by Osler (*Brit. med. J.*, 1885, **1**, 467) to denote aneurysmal dilatations of the arterial wall due to infections within the vascular system.) " Congenital " aneurysms may be particularly liable to become infected, and can be recognized at necropsy by the remnants of their collagenous wall and the neck of the sac. *Fergus R. Ferguson*

993. **Clinical Considerations in the Pathogenesis of Subdural Haematoma.** (Klinische Betrachtungen zur Pathogenese des subduralen Hämatoms)
W. DRESSLER and K. ALBRECHT. *Acta neurochirurgica* [*Acta neurochir. (Wien)*] **5**, 46–67, 1957. 6 figs., bibliography.

As a result of a study of 39 cases of subdural haematoma observed at the University Neurosurgical Clinic, Erlangen, both at operation and by means of encephalographic and arteriographic investigation, the authors conclude that there is a fundamental difference between acute traumatic subdural haemorrhage and chronic subdural haematoma. In their experience if the intracranial pressure remains raised after the injury any haematoma that has formed tends to be absorbed. On the other hand, if there is a general slowing down of the cerebral circulation accompanied by a lowering of intracranial pressure the bleeding tends to persist, and the stage is thus set for the development of a chronic subdural haematoma. *G. S. Crockett*

994. **Chronic Subdural Haematoma.** (Über chronische subdurale Hämatome)
W. BETTAG. *Acta neurochirurgica* [*Acta neurochir. (Wien)*] **5**, 68–81, 1957. 6 figs., 26 refs.

On the basis of histological investigations and the operative findings in 38 cases seen at the University Neurosurgical Clinic, Bonn, the author makes a distinction between chronic encapsulated subdural haematoma of traumatic origin and intradural haematoma—otherwise known as pachymeningitis haemorrhagica interna. [The distinction is largely a pathological one and there seems to be no clear clinical difference between the two types.] The most useful diagnostic procedure is arteriography. The author believes that, at least in the case of intradural haematoma, a lowered intracranial pressure is a factor in the pathogenesis of the disorder. *G. S. Crockett*

995. **Treatment of Paralysis Agitans with Orphenadrine (Disipal) Hydrochloride. Results in One Hundred and Seventy-six Cases**
L. J. DOSHAY and K. CONSTABLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1352–1357, April 13, 1957. 9 refs.

A trial is reported from the Presbyterian Hospital and Columbia University, New York, of "orphenadrine" ("disipal") in the treatment of 176 patients with Parkinsonism, which was post-encephalitic in 30, idiopathic in 75, and arteriosclerotic in 71. The ages of the patients ranged from 36 to 76 years. The dosage of the drug was usually 50 mg. three times a day. In 98 patients there was moderate to marked improvement, but in the remainder the drug was without effect. In some cases it was given in combination with other anticonvulsants, with great benefit. The percentage of patients showing improvement was somewhat higher in the post-encephalitic group than in the others; the drug was least effective when the tremor was marked. Side-effects such as nausea, excitement, and dryness of the mouth were rare and soon disappeared after dosage was reduced. Orphenadrine is a central nervous stimulant and exerts a powerful effect against oculogyric crises, dribbling, and mental depression. The authors conclude that this drug is an invaluable aid in the treatment of paralysis agitans. The chief disadvantage is a tendency for the good effects to wear off after some months; these are not restored by increasing the dose, but may return to some extent on resuming administration after discontinuing the drug for an interval. *G. S. Crockett*

EPILEPSY

996. **Fluctuations of Electrical Activity in the Brain as Related to Epileptic Seizures and Changes of Mood.** (Die Schwankungsbreite hirnelektrischer Erregbarkeit in ihrer Beziehung zu epileptischen Anfällen und Verstimmungszuständen)
G. SCHORSCH and I. VON HEDENSTRÖM. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **195**, 393–407, 1957. 5 figs., 16 refs.

An electroencephalogram (EEG) was recorded daily in 53 cases of epilepsy, 26 idiopathic and 27 symptomatic, at a large epileptic colony at Bielefeld, Germany. Recordings were made at the same hour of the day with the patient at rest and again after 3 minutes' hyperventilation over a period of about 5 weeks. No other special stimulation was used, the authors' purpose being to study the spontaneous changes in the EEG in epilepsy. In each case abnormal features were found in the EEG on at least one occasion.

The most marked abnormalities were found to occur *after* a fit, and lasted sometimes for several days. A reduction of cortical activity was registered immediately *before* the seizure in almost all cases in which such observations were made. A relatively normal EEG was found during depressive mood swings, a finding for which a number of explanations are offered.

[On the whole the evaluation of the results of these careful observations yielded nothing very characteristic or strikingly new concerning the EEG of the institutionalized epileptic.] *W. Mayer-Gross*

997. **Electroencephalographic Changes Induced by the Intravenous Administration of Acetazolamide (Diamox) in Epileptic Patients**
C. SALDÍAS, F. CABIESES, and E. EIDELBERG. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **9**, 333–336, May, 1957. 2 figs., 16 refs.

The authors, working at the National Institute of Neoplastic Disease, Lima, Peru, have studied the immediate effects of intravenous administration of acetazolamide on the electroencephalographic (EEG) recordings from 16 epileptic patients of both sexes, aged between 10 and 55 years. The patients were suffering from various forms of epilepsy, which in most cases was resistant to anticonvulsant therapy, and all had abnormal EEGs. The abnormalities noted consisted in: (1) diffuse slow activity (sometimes paroxysmal and with superimposed spike discharges) (12 cases); (2) a spike or slow

wave focus emerging periodically from a background of normal activity (2 cases); (3) wave-and-spike activity at 3 c.p.s. (one case); or (4) a unilateral focus of slow activity and spikes (one case). The patients were first made to overbreathe for 3 minutes, and 10 minutes later an intravenous injection of 10 mg. of acetazolamide per kg. body weight in 10 ml. of distilled water was given over a period of 15 to 30 seconds. The EEG was then recorded continuously for 30 minutes and hyperventilation was repeated 15 to 30 minutes after the injection. No toxic effects of the drug were observed. In 3 cases EEG abnormalities were suppressed to a striking degree after the injection, while in another 8 the abnormal activity which had appeared after hyperventilation was greatly reduced or suppressed completely. The changes were so rapid that the effect of the drug could not be due to dehydration or acidosis, but must have been the result of a direct action (possibly the inhibition of cerebral carbonic anhydrase) of the drug on the central nervous system. The authors conclude that their results confirm the value of acetazolamide as an anticonvulsant.

John N. Walton

SPINAL CORD

998. **Some Aspects of Cervical Spondylosis**
P. BRADSHAW. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **26**, 177–208, April, 1957. 2 figs., bibliography.

A clinical study of 78 patients with cervical spondylosis and a neurological deficit was carried out at the General Infirmary at Leeds; males outnumbered females by 4 to 1 and the patients' ages varied from 28 to 68. In 55 cases myelopathy was present, sometimes with evidence of root lesions in addition, and in 17 a radiculopathy was present. The average duration of symptoms was 2 to 3 years, during which time steady deterioration was usual. The mode of onset was: in 37 cases with symptoms of cervical root lesions—motor or sensory—with or without the later appearance of a progressive paraplegia; in 19 cases with a progressive paraplegia without sensory disturbance, which might later be followed by involvement of the upper limbs; in 5 cases with simultaneous involvement of the upper and lower limbs; and in the remaining 8 cases with completely atypical symptoms. One-third of the patients had cervical pain with or without radiation to the arms, 25 had brachial pain, and 41 had paraesthesiae most commonly affecting the distal portions of the upper limbs. Clumsiness of upper limb movement and stiffness of the lower limbs were the common motor symptoms.

Examination revealed occasional cranial-nerve abnormalities and limitation of neck movement in 40 patients. The motor signs included wasting, weakness, and fasciculation, with but slight spasticity, in the upper limbs, and in the lower limbs spasticity and disturbance of gait. Reflex abnormalities included extensor plantar responses in all cases of myelopathy, with exaggeration of the tendon reflexes in the lower limb, and absent abdominal reflexes in 50%. In rather less than one-third of the cases abnormality of the reflexes in the upper limb suggested a cervical segmental lesion. The sensory impairment in some cases involved the peripheral parts of the dermatomes in the upper limbs, in others it resembled the suspended and dissociated sensory loss seen in syringomyelia in the lower cervical and upper dorsal dermatomes, and in a third group there was loss of sensibility below a well defined sensory level. Lumbar puncture showed a partial block in 8 cases and a complete block in 2, fluid flow being normal in 61; in 22 cases the protein content of the cerebrospinal fluid was increased to 56 to 200 mg. per 100 ml. On plain radiography typical abnormalities were present in every case, varying in severity, and in all the 77 patients subjected to myelography anterior indentation of the column of opaque medium was present. However, the extent of the neurological disturbance bore little relationship to the degree of abnormality seen on plain films or myelograms.

It is stressed not only that the features of a myelopathy attributable to cervical spondylosis may resemble those of other diseases, but also that the combination of cervical spondylosis and a neurological deficit does not afford assurance that the latter results from the former. Among conditions to be considered in differential diagnosis are motor neurone disease, disseminated sclerosis, subacute combined degeneration of the cord, and syringomyelia, as well as the various lesions outside the spinal canal which involve the motor and sensory innervation of the upper limb.

In considering the importance of trauma it is suggested that: (1) spondylosis localized to a single intervertebral level is indicative of a previous post-traumatic disk protrusion at this level; (2) in the presence of spondylosis trauma may aggravate an existing myelopathy without necessarily giving rise to a disk protrusion; and (3) occupational stress does not appear to predispose to cervical spondylosis, though when the vertebral lesions are present it may increase the risk of a myelopathy developing.

Medical treatment was of little value in cases of myelopathy associated with generalized spondylosis, but improved most cases in which the spondylosis was localized and relieved the majority of those with brachialgia. Surgical treatment carried a mortality of 10%. There was initial improvement, but the disease frequently progressed again after 6 to 18 months—and among those cases in which good results were obtained are included those in which a protrusion of disk tissue had been excised, a procedure which is far more likely to benefit the patient than the laminectomy and division of slips of the dentate ligament which is alone possible in cases of true spondylosis.

It is pointed out that the aetiology of the myelopathy in cervical spondylosis is obscure, and stressed that it is seldom related to direct compression of the cord. Neither does tension applied through the dentate ligaments or constriction by adhesions appear to be responsible for the cord lesion. The possible importance of some mechanism interfering with the blood supply of the cervical cord is discussed.

[This paper is a valuable contribution to the literature dealing with cervical spondylosis.] *J. E. A. O'Connell*

Psychiatry

999. **Repeated Psychometric Evaluations of Preschool Children with Cerebral Palsy**
K. L. KOGAN. *Pediatrics* [*Pediatrics*] **19**, 619–622, April, 1957. 5 refs.

Test scores obtained from 31 children with cerebral palsy at the Spastic Children's Clinic, Seattle, Washington, during a 3-year period are reviewed; all the patients underwent two or more examinations with the Cattell Infant Intelligence Test, the Form L of the Revised Stanford–Binet test, or a combination of these. The standard scoring and method of administering the tests were maintained, items being omitted only when they were such that the child was unable to respond because of his physical handicap. The motor disability is regarded as a part of the equipment of the child as a complete organism and no use is made of hypothetical potential uninfluenced by the handicap. Thus the usual computation of the I.Q., comparing the cerebral palsied child with others of his age group, can predict his educational and social capacity, and training situations can be adjusted accordingly, although his relative strengths and weaknesses must not be ignored.

The changes in the I.Q. scores between the two tests were as follows: second test 10 to 20 points higher in 6 cases (15%), between 9 points higher and 9 points lower in 30 cases (77%), and 10 to 15 lower in 3 cases. The authors point out that these differences can be regarded as attributable largely to the probable error of the I.Q. test scores. Hence it is concluded that for research purposes the I.Qs of cerebral palsied children may have greater validity than has commonly been supposed, and may be no less consistent for these patients than for an unselected population. *J. L. Standen*

1000. **Studies on Phenylketonuria. VI. EEG Studies in Phenylketonuria**
N. L. LOW, J. F. BOSMA, and M. D. ARMSTRONG. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **77**, 359–365, April, 1957. 3 figs., 33 refs.

The authors confirm that nearly all phenylketonuric patients show electroencephalographic (EEG) abnormalities. Thus in a study carried out at the University of Utah College of Medicine, Salt Lake City, it was found that of 94 EEGs recorded from 21 children and 2 adults whose I.Q. ranged from 82 to below 10, only one (that of the oldest subject) was classified as normal by Gibbs's standard. In young phenylketonuric children hypsarrhythmia and multiple-seizure foci are usually found: as the patients grow older the EEG tends to show focal or generalized spike discharges. A history of seizures was obtained in 10 of the present patients, often of the type called " infantile spasms " and described by other authors as petit mal. In general, the younger patients showed severer abnormalities than the older, whether seizures had been grossly apparent or not. Of 5 patients showing improvement in the EEG while on a phenylalanine-restricted diet, 2 showed an increasingly abnormal EEG on interruption of treatment, although in 2 others no remarkable EEG changes were noted.

It is suggested that a phenylalanine-poor diet has beneficial effects on the incidence of seizures and on the EEG in phenylketonuric children, but the authors stress the great variations in the EEG that occur with age, stage of waking, drowsiness, and sleep, and point out that only EEGs obtained under very similar conditions are comparable. In conclusion they suggest that these studies may support the hypothesis of an active process of cerebral damage occurring at an early age which, though no longer continuing in older patients, nevertheless sets a limit to the level of mental capacity eventually attainable. *J. L. Standen*

1001. **Oligophrenia in Combination with Congenital Ichthyosis and Spastic Disorders. A Clinical and Genetic Study.** [In English]
T. SJÖGREN and T. LARSSON. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **32**, Suppl. 113, 1–112, 1957. 15 figs., bibliography.

1002. **The Value of Electroencephalography in Alcoholism**
A. E. BENNETT, L. T. DOI, and G. L. MOWERY. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **124**, 27–32, July, 1956 [received April, 1957]. 4 figs., 9 refs.

At the University of California Medical School, San Francisco, the authors have studied the encephalograms (EEGs) of 95 alcoholics in order to determine the extent to which this procedure may indicate the degree of brain damage in chronic alcoholism. The EEG was recorded on admission in all cases and at least once again in 47 of the cases at varying times thereafter. In 72 out of 93 cases (77·4%) the EEG findings were abnormal, the abnormalities consisting in: (1) fast activity to more or less degree in the frontal and parietal regions, this occurring mainly in cases of acute intoxication, acute hallucinosis, and delirium tremens, and disappearing with clinical improvement; (2) persistent fast activity, slow activity, or spike discharges, these being more frequent in cases of chronic alcoholic deterioration, Korsakoff's psychosis, and in patients with alcoholic convulsions; markedly slow activity was more prevalent in the first two conditions.

From these results the authors infer that transient abnormal EEG findings accompany acute alcoholic states and persistent abnormal findings chronic alcoholic states. From this in turn they conclude that the correlation of the EEG pattern with the clinical course has great significance for the diagnosis and prognosis of alcoholic states, since early organic changes in a given

case may be detected sooner by the persistence of abnormalities in the EEG, even though only the character disorder is apparent. *John A. Clark*

SCHIZOPHRENIA

1003. **The Physiologic Response of Schizophrenic and other Psychotic Patients to a Standard Emotional Stress** G. M. PERRIN and M. D. ALTSCHULE. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 682–688, April 11, 1957. 25 refs.

The theory that " withdrawal from reality " in schizophrenia is characterized by autonomic hyporeactivity was tested by a study of pulse and blood-pressure changes caused by anticipation of shock therapy. It was postulated that if such diminished physiological responsiveness actually does occur in dementia praecox this would be evident on comparing the pulse rate and blood-pressure readings in schizophrenic patients with the same measurements in other psychotic patients.

A total of 96 patients at the McLean Hospital, Waverley, Massachusetts—of whom 9 had catatonic schizophrenia, 11 paranoid schizophrenia, 55 manic-depressive psychosis (13 manic and 42 depressive), and 21 involutional melancholia—were examined. Data from the first 6 treatments of the initial course of electric convulsion therapy in each case were analysed. The average pulse rate and systolic and diastolic pressures rose in all groups before every treatment, and the rises were approximately equal in all the groups. In the patients with manic-depressive psychosis the increases in pulse rate and systolic pressure showed a statistically significant tendency to become greater with succeeding shocks. The implications of this trend were not clear.

It is concluded that the data obtained do not support the theory that there is autonomic hyporeactivity in schizophrenia, and note is taken of the fact that other experiments using emotional stimuli have shown no consistent diminution of vegetative nervous response in dementia praecox. *J. MacD. Holmes*

1004. **Immunological Diagnosis in Schizophrenia** (Иммунобиологическая диагностика шизофрении) G. Y. MALIS. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikiat.*] **57**, 82–86, No. 1, 1957.

The author's previous investigations of the biological properties of the blood of schizophrenic patients (such as its influence on plant growth, the activity of the perfused heart, the growth of tadpoles, and the blood picture in monkeys) have revealed the presence of certain toxic substances in 51·3% of such cases. These substances had certain specific features, and were shown to be neither hormones nor the products of faulty metabolism; nor were they derived from the autonomic nervous system (chemical mediators). On the basis of these and other considerations the author postulated the view that the disorder of the brain in schizophrenia was caused by toxic substances derived from other organs which were infected by a virus. Subsequent investigations, including the present series, have been concerned with a study of the immunological properties of the blood and other body fluids by means of the " A.V.B." reaction (agglutination of virus-laden bacteria). This reaction depends on the property of certain bacteria to adsorb virus particles, and then to be agglutinated by the specific antiserum to that virus.

Altogether 155 patients were studied—90 with schizophrenia of some years' duration and 65 control subjects consisting of patients with a variety of other psychoses and some psychoneurotic and normal subjects. A specific antigen (virus) was found in the blood of 51·1% of the schizophrenics, and specific antibodies to it in a titre of 1:160 or higher were found in 67·5% of this group. The control group gave either negative agglutination reactions or, in a few instances, positive reactions in the lowest dilutions only.

The adsorbent used for the A.V.B. reaction is a non-pigmented strain of *Serratia marcescens* (*Bacillus prodigiosus*) grown for 24 hours in peptone broth at 32° C., and made up into a suspension in normal saline containing 25,000 million organisms per ml., which is then pasteurized for one hour at 58° C. For adsorption of the virus, 1 ml. of the suspension is added to 1 ml. of the patient's serum and the mixture kept at room temperature for an hour with frequent shaking and for 20 hours in a refrigerator (6° C.). It is then washed and centrifuged and the " virus-laden " bacteria made up into a suspension containing 2,000 million organisms per ml., which is used as the antigen. As antiserum the serum of a schizophrenic patient in a state of remission is used. Accuracy of diagnosis and a duration of illness of not less than 12 months are of paramount importance. The agglutination reactions are carried out in the usual way, 1 ml. of the diluted antiserum and 2 drops of the antigen being used; the tubes are incubated for 3 hours at 37° C. and then kept in a refrigerator for 40 hours before reading. *Alexander Duddington*

TREATMENT

1005. **Bimedial Lobotomy: Five-year Evaluation** N. PAUL, E. FITZGERALD, and M. GREENBLATT. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **124**, 49–52, July, 1956 [received April, 1957]. 3 figs., 1 ref.

The study here reported from the Boston Psychopathic Hospital (Harvard Medical School), Boston, was designed to compare the therapeutic effectiveness of three lobotomy procedures, namely, bimedial, unilateral, and full bilateral lobotomy performed respectively on 35, 42, and 39 (total 116) chronic mentally ill patients. The clinical results at one year revealed superiority of the bimedial operation. The same patients have now been re-investigated 5 years after lobotomy to determine which, if any, of the three operative procedures is preferable with respect to long-term clinical results.

It is stated that: " in substance the 5-year re-investigation confirms the superiority of bimedial over bilateral and unilateral lobotomy and also establishes the fact that, by and large, post-lobotomy gains visible at one year are generally sustained to 5 years ". Over-

all improvement to a " significant " level was seen in 23 (65%) of the bimedially operated group, compared with 17 (44%) of the full bilateral group and 13 (31%) of the unilateral group. It was found that patients subjected to bimedial lobotomy exhibited greater improvement in work activity in the postoperative period as compared with such activity preoperatively than did those treated by either full bilateral or unilateral lobotomy: thus at 5 years 54% of the bimedial cases were rated as showing " good " work adjustment compared with 33% of the bilateral group and 29% of the unilateral group. The authors also note that there was a real increase in the number of patients showing " good " work adjustment on re-investigation in the bimedial group compared with the other two groups, the percentage gains in work adjustment showing that the " improvement potential " in this group was not fully realized at the end of one year but continued to emerge during the next 4 years. *John A. Clark*

1006. **Effects of Promazine in Mental Syndromes**
H. AZIMA and H. DUROST. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 442–446, March 15, 1957. 8 refs.

1007. **Clinical Evaluation of Chlorpromazine Therapy for Mental Illnesses. Analysis of One Year's Experience**
P. E. FELDMAN. *Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology* [*J. clin. exp. Psychopath.*] **18**, 1–26, Jan.–March, 1957. 5 figs., 17 refs.

The author reports the experience of 37 physicians at Topeka State Hospital, Kansas, in the administration of chlorpromazine to 321 patients (average age 46½ years, average time in hospital 9 years), 74% of whom had schizophrenia, 13% chronic brain syndromes, 4·4% manic-depressive reactions, 2·9% involutional psychotic reactions, and the remainder behaviour disorders, psychoneuroses, and mental deficiency. The drug was administered orally, intramuscularly, or intravenously. Treatment by physical methods and by psychotherapy was continued concomitantly. Each patient's improvement was assessed on a 4-point scale for 24 separate items and an over-all assessment was made on a 6-point scale, usually after 4 to 7 months' medication.

Adequate therapeutic effects appeared, irrespective of the method of administration, at a dosage of 200 to 250 mg. per day. Most of the physicians administered the drug 3 times a day, gradually increasing the dose every 3 to 7 days by 50 to 100 mg. until the optimum level was reached, after which the dosage could be reduced in some cases without loss of effect. General improvement was classified as " marked " in 24·1% and " moderate " in 41·4% of the patients. Only 6·4% failed to derive some benefit. Of 238 schizophrenics, 9% showed " marked ", 25·5% " moderate to marked ", and 17·5% " moderate " improvement. On the whole in this group the shorter the illness, the more beneficial the therapy, though 52% of those schizophrenics who had been ill for longer than 10 years still responded favourably. Seven of the 9 patients in the manic phase of manic-depressive psychosis showed " moderate to marked " improvement and one of 3 in the depressive phase showed " moderate " improvement. Only one of 9 patients with involutional psychotic reactions failed to show at least " moderate " improvement, and of 42 with organic brain syndromes, 43% showed " marked to moderate " improvement. In many cases symptoms which had hitherto prevented patients of the latter class being boarded out were eliminated or ameliorated.

Only one-third of all patients improved in insight and less than half in judgment. Of 120 with defect of memory, 56% showed improvement, and of 150 with orientation defects, 62% responded in some degree. Almost two-thirds of 242 patients with defects in affect improved to some degree. Compulsiveness did not respond so well as other defects, but over one-half of the patients with this disorder showed some improvement. Some improvement in respect of self-mutilation occurred in 67·5%. About half of 201 patients with delusions showed " moderate to marked " improvement. Of 149 patients with anorexia, 85% showed definite improvement. Improvement was also recorded in respect of inaccessibility in 84·5% of 249 patients, mannerisms in 108 of 145 schizophrenics, sleep in 83·5% of all patients, and negativism in 89·5% of 257 patients. For 94 out of 119 patients hallucinations were completely eliminated or were reduced in intensity and frequency, 203 out of 226 patients showed some improvement in respect of hostility, and 180 out of 193 showed reduction in hyperactivity. Only 19 out of 168 failed to improve in respect of combativeness.

Side-effects of 21 different types occurred in 135 patients, and 7 patients developed untoward depression. There were 2 suicides in the series, and although there was no evidence to relate these to the medication, the authors advise against complacency in chlorpromazine therapy. The most common side-effect was drowsiness (22·8% of 321 patients), mostly not persisting beyond 7 to 10 days and, when profound, eliminated by giving 5 to 10 mg. of dextroamphetamine. Parkinsonism in 12 cases (3·8%) appeared to be a manifestation of high dosage. Skin rashes also occurred in 12 cases and responded well to antihistaminics except in 3 in which cortisone was required. Dizziness and hypotension each occurred in 9 cases (2·8%) and depression in 7 (2·2%). No serious case of cardiovascular collapse was noted. Jaundice occurred in 6 cases (1·9%), and in 6 others the leucocyte count fell significantly during medication, returning to normal when it was discontinued. There were 6 cases of vomiting and 6 of increased turbulence requiring discontinuance of the drug. No other side-effects affected more than 1% of the patients treated.

Hours of seclusion and restraint have declined during the year of the study. Most patients responded to 200 to 250 mg. daily—some to as little as 30 and others only to 2,500 mg. daily. A small group of 14 patients were given combined chlorpromazine and reserpine treatment in a dosage ratio of 100:1, all being " moderately to markedly " improved.

[No control group was used and no descriptive statistics or tests of significance are given.] *John C. Kenna*

Dermatology

1008. **Benign Polyarteritis Cutanea.** (Über die Polyarteriitis cutanea benigna)
P. CERUTTI and G. SANTOJANNI. *Hautarzt* [*Hautarzt*] 8, 109–118, March, 1957. 12 figs., 38 refs.

The case histories of 8 patients who attended the Skin Clinic of the University of Naples with either indolent skin nodules or haemorrhagic bullae and subsequent ulceration are presented. Histologically, polyarteritis nodosa was diagnosed. In 2 cases systemic involvement was present, but in the others the condition appeared to be confined to the skin. It is suggested that there exists a chronic benign form of cutaneous polyarteritis nodosa without systemic involvement. *G. W. Csonka*

1009. **The Treatment of Lupus Erythematosus and Lymphocytic Infiltration of the Skin with A.P.A. 5533**
C. R. REIN and R. FLEISCHMAJER. *British Journal of Dermatology* [*Brit. J. Derm.*] **69**, 174–177, May, 1957. 7 refs.

A combination of mepacrine, chloroquine, and "plaquenil" (hydroxychloroquine; A.P.A. 5533) was given to 10 patients with chronic lupus erythematosus and 4 with lymphocytic infiltration of the skin, the treatment regimen being based on an initial high dosage. The results were found to be better than those obtained with each drug given individually. A number of patients had severe or mild side-effects, including diarrhoea, diplopia, and vertigo. *John T. Ingram*

1010. **Cutaneous Reticuloses (Histiomonocytic Reticuloses).** (Réticuloses cutanées (Réticuloses histiomonocytaires))
R. DEGOS, B. OSSIPOVSKI, J. CIVATTE, and R. TOURAINE. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **84**, 125–152, March–April, 1957. 16 figs., bibliography.

In this communication from the Hôpital Saint-Louis, Paris, the authors define the cutaneous reticuloses as proliferations of reticulo-histiocytic elements in the skin which form dense, homogeneous, persistent dermal infiltrates with a tendency to extend and spread. Their monomorphic homogeneous nature distinguishes them from the granulomatoses, but the occasional presence of a different type of cell does not invalidate the diagnosis. These features also distinguish cutaneous reticuloses from reticular reactions (hyperplastic reticuloses) occurring in a variety of conditions. In some cases a reticular reaction may precede a true cutaneous reticulosis. Reticulum-cell sarcoma of the skin is included in this definition because the distinction between metaplasia and neoplasia appears unjustifiable. Further extension to include involvement of the bone marrow and the blood also brings certain leukaemias into this definition. Thus hyperplastic reticulosis proceeding to malignant reticulosis or reticulum-cell sarcoma and monocytic leukaem a may, but need not, be successive stages of the same process.

Clinically, cutaneous reticuloses usually run a chronic or subacute course, the lesions resembling mycosis fungoides and cutaneous leukaemias. The absence of pruritus and the appearance of nodules without preceding erythema are in favour of reticulosis. The final diagnosis is based on repeated histological examination and the study of fresh smears of biopsy specimens ("dermograms") stained by the May–Grünwald–Giemsa technique, lymph-node biopsy, and also the myelogram and haematogram. The position of hyperplastic reticulosis is the most debatable, and this is discussed in detail. The authors believe that this condition, if followed up long enough, in some cases even after several remissions and relapses, will prove to be malignant. In one such case a reticulum-cell sarcoma of the stomach developed after a 30-year history of nodular cutaneous hyperplastic reticulosis.

Malignant cutaneous reticuloses may be associated with leukaemia, most often of a histio-monocytic form, and in regard to skin and lymph nodes the more immature cell types herald a more rapid evolution. A lymphomonocytic leukaemia occurs more rarely; in this, first the one and then the other cell-type may account for 50 to 70% of the nucleated cells. In some of the authors' cases a simultaneous parallel course of histio-monocytic and of lymphoid proliferation is assumed. The dermatological aspect of cutaneous reticuloses is sometimes complicated during the leukaemic phase by purpura, mucosal lesions, and infection. The acute forms of malignant cutaneous reticuloses are briefly discussed. Malignant change in pre-existing skin disease is mentioned and 5 cases of malignant reticulosis and 2 of mycosis fungoides occurring 3 to 22 years after the onset of a true psoriasis are quoted. The nosological separation of Hodgkin's disease from malignant reticulosis is favoured, although histologically a Hodgkin sarcoma may present the appearance of a monomorphic reticulum-cell sarcoma. The same argument applies to the granulomatous and sarcomatous types of mycosis fungoides.

In the authors' clinic treatment for simple hyperplastic lesions is withheld unless severe pruritus requires corticotherapy or deep *x*-ray therapy. In the malignant phase the latter is favoured, and dosages are suggested. Radioactive isotopes have given disappointing results in the authors' hands. Corticotherapy is followed by earlier relapses and there is a risk of deterioration under treatment, but it can sometimes restore lost radiosensitivity. Leukaemic forms are a contraindication to the use of radiotherapy, but they may benefit from corticoids and maybe also 6-mercaptopurin. The authors have successfully treated erythrodermic skin infiltrates by painting daily with coal-tar. One case of ulcero-tumoral reticulosis has for the time being been successfully treated surgically, followed by skin grafting. *F. Hillman*

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Paediatrics

1011. **Evaporated Milk in Infant Feeding**
P. D. Moss. *British Medical Journal* [*Brit. med. J.*] **1**, 1453–1455, June 22, 1957. 11 refs.

The occurrence of 8 outbreaks of food poisoning in one month caused by staphylococcal enterotoxin contained in spray-dried milk has recently been reported (Anderson and Stone, *J. Hyg.* (*Lond.*), 1955, **53**, 387; *Abstracts of World Medicine*, 1956, **19**, 494). The present author claims that evaporated tinned milk is free from any such risk of contamination. The milk as received from the farm is first treated at 100° C. during solids stabilization and later at 115·5° C. for 15 minutes. No milk remains in any heating chamber for more than 15 minutes between heating processes, ensuring that no spores or living organisms, particularly staphylococci, can survive, while staphylococcal enterotoxin cannot be produced by a " build-up " of staphylococci during processing, as may happen with spray-dried milk.

Other advantages of evaporated milk for infant feeding are that it mixes easily, does not block teats, and does not deteriorate during keeping. In addition there appears to be a lower incidence of sore buttocks during its use. Premature infants can be fed successfully on it. Although it appears to be more expensive than dried milk, there is usually less wastage. One difficulty is in remembering a formula for its use. One-third evaporated milk, two-thirds water, and a level teaspoonful (4 g.) of sugar to every 4 fl. oz. (114 ml.) gives a mixture providing 20 Calories per fl. oz. (0·715 Cal. per ml.). It is wise to supplement the feed with some form of vitamin concentrate even if vitamin D is added to the milk in processing. The author considers that evaporated milk is safe and satisfactory for infant feeding, but he nevertheless emphasizes that " the first choice of feed is always breast milk ". *J. G. Jamieson*

NEONATAL DISORDERS

1012. **The State of Development of Newborn African Children**
M. Geber and R. F. A. Dean. *Lancet* [*Lancet*] **1**, 1216–1219, June 15, 1957. 6 figs., 6 refs.

The authors studied the state of development of 107 normal newborn infants of the Ganda and other tribes seen in the maternity department of Mulago Hospital, Kampala, the technique of neurological examination used being that of André Thomas. At birth muscle development (especially of the head and neck) of the African infants was advanced, primitive reflexes were frequently absent, and the general status of development corresponded to that of European babies aged 4 to 6 weeks. This advanced degree of development was common to all the indigenous tribes and was uninfluenced by sex, birth weight, or the parity of the mother. The state of development of 15 European and 60 Indian infants also born in Kampala was found to be similar to that of infants born in Europe. *R. M. Todd*

1013. **The Transfer of Blood between Baby and Placenta in the Minutes after Birth**
M. Gunther. *Lancet* [*Lancet*] **1**, 1277–1280, June 22, 1957. 7 figs., 17 refs.

In a study at University College Hospital, London, of the transfer of blood between the infant and the placenta, the weights of 50 infants were recorded continuously on rotating drums from birth until just before the birth of the placenta. Of the 50 infants, 33 males and 17 females, 39 were born vaginally and 11 by Caesarean section. It was observed that while the blood flow was usually towards the infant in the vaginal deliveries, the opposite occurred quite often. To study the effect of siphonage, the weighing machine and the infant were raised or lowered 15 cm. from the level of the vulva. In 5 of the 19 instances in which this was carried out there was clear evidence of loss or gain through venous siphonage. Of the infants born by Caesarean section, 3 were large and vigorous and showed considerable weight gain, but even the smaller infants showed a gain in weight. From these observations the author concludes that if the cord is left untied the infant will acquire a weight of blood ranging from 0·8% to 4·7% of body weight. Attention is drawn to the possible action of the pulmonary vessels with the onset of respiration, the effect of pressure changes in the circulation, and the part played by the patency of the foramen ovale and the ductus arteriosus. The duration of pulsation in the cord was found to be prolonged when the mother received analgesia, and this, it is suggested, may have a bearing on the closure of the ductus arteriosus.
David Morris

1014. **The Effect of Rh Genotypes on Severity in Haemolytic Disease of the Newborn**
S. Murray. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 143–152, April, 1957. 2 figs., 15 refs.

The Rh genotypes of the fathers of 540 babies with haemolytic disease of the newborn were determined at the Regional Blood Transfusion Centre, Newcastle upon Tyne, with anti-C, anti-D, anti-E, anti-c, and anti-e antisera. The abnormally high frequency of D/D homozygotes among the fathers of affected babies was confirmed, and among the three commoner homozygous D genotypes, R_1R_2, R_1R_1, and R_2R_2, there was found a significant excess of the types containing R_2 (cDE). It is claimed that there is an increased risk of immunization if the husband has the R_2 chromosome, and that the outlook is better initially for the wife of an R_1R_1 husband. The calculated risk for the wives of heterozygous husbands is 1 in 32 and for wives of homozygous

husbands 1 in 15; of the latter, the risk for the wives of R_1R_1 husbands is 1 in 17, compared with 1 in 14·7 where the husband is R_1R_2 and 1 in 9·6 with an R_2R_2 husband.

A suggestive excess of R_2r babies was found among those with severe disease, and the proportion of R_2R_2 fathers was high in cases of stillbirth. The "family pattern" in which there is a sequence of mildly affected babies or of stillbirths can be partly explained on a basis of the genotype of the father.

It is suggested that the presence of the R_2 chromosome in the father is an unfavourable finding, and may be used as a further indication for such treatment as early induction of labour. *John Murray*

1015. **Combined Rh and AB Hemolytic Disease of the Newborn**

H. H. GUNSON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **27**, 35–41, Jan., 1957. 6 refs.

Four cases of haemolytic disease of the newborn are described in which the babies were of Group A and their mothers of Group O. The serum of 3 of the babies gave a positive indirect Coombs reaction with adult Group-A_1 Rh-negative erythrocytes. Sera were also tested from 47 normal Group-A babies of Group-O mothers, and of these only 2 gave a positive indirect Coombs reaction with erythrocytes of Group A_1 or B; these 2 infants subsequently developed haemolytic disease.

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A low but significant correlation between cord blood oxygen saturation and clinically observed anoxia was found. There was, however, no relationship between immediate postnatal anoxia and the blood oxygen level at one hour. There was also no relationship between oxygen saturation and the performance in the behaviour tests, and no difference in the performance in these tests between two extreme groups selected on the basis of oxygen levels. It is concluded that estimation of oxygen saturation does not provide an objective measure of neonatal anoxia, and that the cord blood sample, which should be the most revealing of the oxygen economy of the infant at birth, is unreliable as a predictor of later oxygen status. *Marianna Clark*

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Candida albicans cannot be regarded as a normal constituent of the microbial flora of the newborn infant. The presence of blastospores in oral smears from the third or fourth day of life onward permits prediction of clinical oral thrush within one to five days with almost 100% certainty. Oral thrush is present or imminent as soon as hyphae are found in direct oral smears. The presence of *C. albicans* in the intestine of the newborn infant is closely associated with clinical candidiasis and predisposes to cutaneous lesions in the perianal and diaper area.

In view of these findings, we advocate routine swabbing of the newborn's mouth on the fourth day of life in order to detect potential cases of oral thrush. Treatment should be instituted when spores are found, and is definitely indicated if hyphae are present. Preferably such treatment should consist in oral rather than in topical medication in order to eliminate the organism from the digestive tract and to prevent cutaneous candidiasis resulting from contact with the infected feces.—[Authors' summary.]

1018. **Small Intestine Obstruction in the Newly Born**

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An account of the common causes of intestinal obstruction in the newborn and the appropriate treatment is given. The author's conclusions are as follows.

"Provided that the upper distended loop is resected or adequately decompressed, atresia can be relieved by surgical means. Satisfactory surgical techniques have been developed, but the results of treatment of neonatal obstruction will improve only when: (1) All babies who vomit bile or vomit persistently are investigated immediately. (2) The diagnosis is made before the vitality of the gut is impaired or post-natal perforation occurs. (3) The surgeon not only relieves the obstruction but also takes adequate steps to exclude multiple lesions distal to it. (4) The majority of these babies are cared for in units, the staff of which are trained in the special care of newborn and premature infants.

"In the post-operative period care must be taken to control the fluid and electrolyte therapy, the usual tendency being to over rather than under treat these small babies. Despite most careful treatment and even

Paediatrics

1011. **Evaporated Milk in Infant Feeding**
P. D. Moss. *British Medical Journal* [*Brit. med. J.*] **1**, 1453–1455, June 22, 1957. 11 refs.

The occurrence of 8 outbreaks of food poisoning in one month caused by staphylococcal enterotoxin contained in spray-dried milk has recently been reported (Anderson and Stone, *J. Hyg.* (*Lond.*), 1955, **53**, 387; *Abstracts of World Medicine*, 1956, **19**, 494). The present author claims that evaporated tinned milk is free from any such risk of contamination. The milk as received from the farm is first treated at 100° C. during solids stabilization and later at 115·5° C. for 15 minutes. No milk remains in any heating chamber for more than 15 minutes between heating processes, ensuring that no spores or living organisms, particularly staphylococci, can survive, while staphylococcal enterotoxin cannot be produced by a " build-up " of staphylococci during processing, as may happen with spray-dried milk.

Other advantages of evaporated milk for infant feeding are that it mixes easily, does not block teats, and does not deteriorate during keeping. In addition there appears to be a lower incidence of sore buttocks during its use. Premature infants can be fed successfully on it. Although it appears to be more expensive than dried milk, there is usually less wastage. One difficulty is in remembering a formula for its use. One-third evaporated milk, two-thirds water, and a level teaspoonful (4 g.) of sugar to every 4 fl. oz. (114 ml.) gives a mixture providing 20 Calories per fl. oz. (0·715 Cal. per ml.). It is wise to supplement the feed with some form of vitamin concentrate even if vitamin D is added to the milk in processing. The author considers that evaporated milk is safe and satisfactory for infant feeding, but he nevertheless emphasizes that " the first choice of feed is always breast milk ". *J. G. Jamieson*

NEONATAL DISORDERS

1012. **The State of Development of Newborn African Children**
M. Geber and R. F. A. Dean. *Lancet* [*Lancet*] **1**, 1216–1219, June 15, 1957. 6 figs., 6 refs.

The authors studied the state of development of 107 normal newborn infants of the Ganda and other tribes seen in the maternity department of Mulago Hospital, Kampala, the technique of neurological examination used being that of André Thomas. At birth muscle development (especially of the head and neck) of the African infants was advanced, primitive reflexes were frequently absent, and the general status of development corresponded to that of European babies aged 4 to 6 weeks. This advanced degree of development was common to all the indigenous tribes and was uninfluenced by sex, birth weight, or the parity of the mother. The state of development of 15 European and 60 Indian infants also born in Kampala was found to be similar to that of infants born in Europe. *R. M. Todd*

1013. **The Transfer of Blood between Baby and Placenta in the Minutes after Birth**
M. Gunther. *Lancet* [*Lancet*] **1**, 1277–1280, June 22, 1957. 7 figs., 17 refs.

In a study at University College Hospital, London, of the transfer of blood between the infant and the placenta, the weights of 50 infants were recorded continuously on rotating drums from birth until just before the birth of the placenta. Of the 50 infants, 33 males and 17 females, 39 were born vaginally and 11 by Caesarean section. It was observed that while the blood flow was usually towards the infant in the vaginal deliveries, the opposite occurred quite often. To study the effect of siphonage, the weighing machine and the infant were raised or lowered 15 cm. from the level of the vulva. In 5 of the 19 instances in which this was carried out there was clear evidence of loss or gain through venous siphonage. Of the infants born by Caesarean section, 3 were large and vigorous and showed considerable weight gain, but even the smaller infants showed a gain in weight. From these observations the author concludes that if the cord is left untied the infant will acquire a weight of blood ranging from 0·8% to 4·7% of body weight. Attention is drawn to the possible action of the pulmonary vessels with the onset of respiration, the effect of pressure changes in the circulation, and the part played by the patency of the foramen ovale and the ductus arteriosus. The duration of pulsation in the cord was found to be prolonged when the mother received analgesia, and this, it is suggested, may have a bearing on the closure of the ductus arteriosus.
David Morris

1014. **The Effect of Rh Genotypes on Severity in Haemolytic Disease of the Newborn**
S. Murray. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 143–152, April, 1957. 2 figs., 15 refs.

The Rh genotypes of the fathers of 540 babies with haemolytic disease of the newborn were determined at the Regional Blood Transfusion Centre, Newcastle upon Tyne, with anti-C, anti-D, anti-E, anti-c, and anti-e antisera. The abnormally high frequency of D/D homozygotes among the fathers of affected babies was confirmed, and among the three commoner homozygous D genotypes, R_1R_2, R_1R_1, and R_2R_2, there was found a significant excess of the types containing R_2 (cDE). It is claimed that there is an increased risk of immunization if the husband has the R_2 chromosome, and that the outlook is better initially for the wife of an R_1R_1 husband. The calculated risk for the wives of heterozygous husbands is 1 in 32 and for wives of homozygous

husbands 1 in 15; of the latter, the risk for the wives of R_1R_1 husbands is 1 in 17, compared with 1 in 14·7 where the husband is R_1R_2 and 1 in 9·6 with an R_2R_2 husband.

A suggestive excess of R_2r babies was found among those with severe disease, and the proportion of R_2R_2 fathers was high in cases of stillbirth. The "family pattern" in which there is a sequence of mildly affected babies or of stillbirths can be partly explained on a basis of the genotype of the father.

It is suggested that the presence of the R_2 chromosome in the father is an unfavourable finding, and may be used as a further indication for such treatment as early induction of labour. *John Murray*

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"In the post-operative period care must be taken to control the fluid and electrolyte therapy, the usual tendency being to over rather than under treat these small babies. Despite most careful treatment and even

with early diagnosis there will always be a mortality rate in these cases because of multiple intestinal anomalies or congenital defects in other systems but the prognosis in solitary lesions should be a normal expectancy of life." *Charles Nicholas*

CLINICAL PAEDIATRICS

1019. **Physical and Mental Handicaps following a Disturbed Pregnancy**
D. H. STOTT. *Lancet* [*Lancet*] **1**, 1006–1012, May 18, 1957. 21 refs.

From the University of Bristol the author presents an analysis of the antecedents, in regard to health during the first 3 years of life and abnormal events during pregnancy, of 65 educationally subnormal children with a mean I.Q. of 66 and 40 mental defectives with an I.Q. of 50 or less who were chosen " as being of normal appearance " from among those attending an occupation centre. In 55 cases the information available included notes from health visitors' cards and in each case the mother was interviewed. Controls were chosen as follows: (1) 91 children under 19 years of age who were siblings of the defective children, but were not themselves defective; (2) 111 children, nearly all of average ability, and 22 children of parents attending an adult education centre; and (3) 144 children of professional case-workers and 82 normal siblings of another sample of mentally handicapped children.

It was found that ill health was about three times more frequent in the histories of the retarded group than in those of the controls. [Some of the illnesses listed, however, such as " failure to gain ", " ailing in the first months ", and " thyroid deficiency ", are merely well recognized features of mental deficiency. Thyroid deficiency would not be regarded as an illness in a cretin, and it would not be found in other mental defectives.] There was a close association between illness or stress in the mother during pregnancy and illness in the child during the first 3 years. Where illness or stress during pregnancy was reported, 76% of the children had had at least one of the illnesses listed, as against 29% of those children in respect of whom no pregnancy trouble had occurred. Pregnancy illness or stress was reported in respect of 66% of the retarded children and of only 30% of the controls. [Pregnancy troubles included severe matrimonial troubles, including those related to alcoholism, problem families, and illegitimacy. It may be thought that these might be related to a low I.Q. in the parents and so to a low I.Q. in the child.] There were congenital malformations in 15% of the retarded children and 1·5% of the controls.

The author concludes that there is evidence of a syndrome with the following components. (1) Early ill health, the child having one or more of the following characteristics: generally ailing or a failure to gain weight in the first months; subject to nutritional or respiratory disease or local infection; underweight but not premature at birth. (2) Mental retardation, in most cases from birth. (3) Congenital malformation.

[This paper is interesting, but the value of the author's conclusions is difficult to assess because of the numerous factors concerned. The accuracy of the data must also be questioned, because of their dependence on the memory of mothers about events as far as 19 years back.] *R. S. Illingworth*

1020. **Some Observations on 1,246 Cases of Geographic Tongue. The Association between Geographic Tongue, Seborrheic Dermatitis, and Spasmodic Bronchitis—Transition of Geographic Tongue to Fissured Tongue**
P. RAHAMIMOFF and H. V. MUHSAM. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **93**, 519–525, May, 1957. 2 figs., 10 refs.

Over a period of 5 years following the establishment of the State of Israel 1,246 cases of geographical tongue were observed in Jaffa out of a total of 8,305 children examined—an incidence of 15%. The present paper is largely concerned with children under 2 years of age, numbering 5,425, among whom the incidence of geographical tongue was 775 (14·29%). A close study suggested that there was some association between the three conditions of geographical tongue, seborrhoeic dermatitis, and spasmodic bronchitis, it being postulated that all three are in some way the result of a reaction to common environmental stimuli. The fact that in 41 instances the condition of geographical tongue was later replaced by fissured tongue was taken to indicate that a relationship exists between the two. *John Fry*

1021. **The Electrolyte Content of the Sweat in Fibrocystic Disease of the Pancreas**
B. W. WEBB, P. T. FLUTE, and M. J. H. SMITH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 82–84, April, 1957. 3 figs., 2 refs.

A method for the collection of specimens of sweat is described and the sodium and chloride content of sweat from control subjects and fibrocystic patients have been measured. The electrolyte content of sweat from fibrocystic patients is significantly higher than that of sweat from the control subjects.—[Authors' summary.]

1022. **A Study of Infantile Colic**
W. C. TAYLOR. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 458–461, March 15, 1957. 2 refs.

The author has reviewed the records of 100 babies with " three-month colic " seen in a paediatric practice in Winnipeg and compared them with those of a similar number of infants without colic. The syndrome, which typically occurs in infants under 3 months of age, is characterized by recurrent attacks of crying or screaming without obvious cause, these attacks often being rhythmic, recurring every 5 to 10 minutes, but sometimes being continuous and accompanied by drawing up of the knees, sweating, and other signs of pain; they are usually worse in the evening. In the present series the symptoms varied from mild to severe; none of the infants with colic showed any signs of physical disease when first seen. Approximately 45 infants in each group were followed up to the age of 5 years.

There was no difference in sex incidence between the patients and controls, and differences in feeding regimens were slight, 23 babies with colic being fully breast-fed compared with 30 controls, and 46 receiving breast milk plus complementary feeds compared with 33 controls. (The author suggests that the mothers of colicky babies may have changed the feeds in the hope of alleviating symptoms, but this point was not investigated.) Cereal was generally added at 2 to 3 months of age and the symptoms usually disappeared at about this time, but earlier introduction of solids produced no improvement in the colic, while larger milk feeds resulted in only temporary relief. It was noted nevertheless that in babies with colic the average weight gain at 3 months was 6 oz. (170 g.) more than in the controls, and 1 lb. (450 g.) more at 7 months of age.

There was no notable difference in the incidence of regurgitation, vomiting, constipation, diarrhoea, transient skin rashes, eczema, rhinitis, or reactions to inoculation between the two groups, but asthma was more prevalent in the control group. Three babies with colic and one in the control group later developed febrile convulsions. One baby with colic subsequently had breath-holding attacks, but generally there was no difference later in the incidence of minor behaviour difficulties. Of the 100 mothers of babies with colic, 12 appeared to be tense, anxious, and emotionally unstable compared with only 2 mothers of control infants. Infantile colic was not more common in first babies, but the family history showed that in 41 of the cases a sibling also had had colic, whereas this was noted in only 28 of the controls. In 83% of the patients the symptoms developed before the age of 4 weeks, and in 88% had disappeared by the age of 3 months; there was no seasonal incidence. In 49% the colic was most severe between 6 and 10 p.m. Treatment was with phenobarbitone ($\frac{1}{8}$ to $\frac{3}{8}$ grain; 8 to 24 mg.) before each feed and liberal milk feeding was allowed. Attempts were also made to reduce emotional tension in the home and to reassure the mother.

[The author's study has not revealed the cause of this puzzling condition which, although benign, can be a great worry to parents. The familial tendency and the higher weight gain in the patients compared with controls are of interest.] *Pamela Aylett*

1023. **Operative Treatment of Cerebral Palsy Involving the Lower Extremities**

C. M. SILVER and S. D. SIMON. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **27**, 457–465, April, 1957. 2 figs., 13 refs.

This paper presents a study of spastic children with cerebral palsy who have undergone various operations at Miriam Hospital, Providence, Rhode Island, for deformities of the lower extremity, a total of 177 operations being performed on 57 patients aged 19 months to 13 years. The age of the child, his mental state, and the various operative procedures available are discussed. In the case of the hip-joint, adductor tenotomy or Soutter's operation for flexion contracture of the hip may be tried. Operations for flexion contracture of the knee, such as advancement of the gastrocnemius and lengthening of the tendo Achillis for equinus deformity of the ankle, are also described.

Throughout the paper the authors stress that in these cases team work is necessary, and surgery should not be considered until exhaustive diagnostic studies have been made. Only then should definite clinical spastic deformities be operated on, and surgery under these conditions gives good results. But it is pointed out that these operations are merely one item in the comprehensive programme of treatment required for cerebral palsy in children. *Leon Gillis*

1024. **Kernikterus not Associated with Haemolytic Disease**

WONG HOCK BOON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 85–90, April, 1957. 1 fig., 21 refs.

Twenty-six cases of kernikterus of non-haemolytic origin in the newborn infant occurring in the Paediatric Unit of the General Hospital, Singapore, during the period March, 1955, to December, 1955, are described.

The incidence of these cases in full-term, mature infants as distinct from previous reports mainly in premature infants is stressed.

The mechanism of kernikterus in general is briefly described and the probable mode of the production of kernikterus in the present series discussed. It is suggested that in some of these cases the offending pigment, which is the " indirect bilirubin ", is excessively raised as a result of the normal physiological breakdown of red cells after birth superimposed on an inefficient liver due to protein malnutrition in the mother. Sepsis may have been a contributory factor.—[Author's summary.]

1025. **Metharbital (Gemonil) in Myoclonic Spasms of Infancy and Related Disorders**

M. A. PERLSTEIN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **93**, 425–429, April, 1957. 4 refs.

In this paper from Cook County Hospital and Northwestern University Medical School, Chicago, the author reports further experience with metharbital (" gemonil "), a non-toxic barbiturate, in the treatment of epilepsy and spasticity. The drug was found to be of practically no value in reducing spasticity or tension in patients with cerebral palsy. It was, however, effective in reducing the frequency of epileptic attacks, especially when these were associated with organic disease of the brain, when it was 7 times more effective than in idiopathic epilepsy. It proved of most use in the control of myoclonic spasms in infants, 66% of such patients benefiting. There were no side-effects, apart from some somnolence and an unsteadiness of gait when the drug was given in large doses, and a rash (2 cases) which disappeared within 48 hours of ceasing administration of the drug.

J. W. Aldren Turner

1026. **Two Cases of Listerial Meningitis in Infants**

P. N. EDMUNDS, D. N. NICHOLSON, and D. M. DOUGLAS. *British Medical Journal* [*Brit. med. J.*] **2**, 188–191, July 27, 1957. 23 refs.

Medical Genetics

1027. **Blood Chimerism in a Pair of Twins**
P. B. Booth, G. Plaut, J. D. James, E. W. Ikin, P. Moores, R. Sanger, and R. R. Race. *British Medical Journal* [*Brit. med. J.*] **1**, 1456–1458, June 22, 1957. 1 fig., 15 refs.

The authors describe the blood groups (ABO, MNSs, P, Rh, Luther, Kell, Lewis, Duffy, and Kidd) of a family of 2 parents and 3 children, including twins of opposite sex, to which their attention was directed by the occurrence of a weak anti-A reaction in tests of blood donated by the female twin at the North London Blood Transfusion Centre, Edgware. Nothing unusual was detected in the grouping of the blood of the parents or of the twins' brother, but both twins were shown to have mixed erythrocytes; in the female the proportions of the two components were estimated as 99% Group O and 1% Group A, and in the male as 14% Group O and 86% Group A_1. The two components also differed in the ABO, MNSs, Rh, Duffy, and Kidd systems. [For details of the full typing of the whole family and of each component of the twins and of the tests used the original paper should be consulted.] Thus the ancestral erythrocytes of each twin came from two sources: (1) cells inherited from the parents, and (2) cells grafted *in utero* from the other twin. Tests of saliva showed that the male twin secreted A and H antigens and the female the H antigen. The genetic groups of the male were therefore those of the A series and of the female those of the O series.

In addition, " drumstick " nodules were found on the nuclei of some of the polymorphonuclear leucocytes of the male twin, and since these are normally limited to females, it is assumed that ancestral leucocytes must also have crossed from the female twin. A review of the literature on blood chimerism is included, together with a critical examination of the tests used in the present work. *E. A. Cheeseman*

1028. **Human Blood Chimeras. A Study of Surviving Twins**
J. W. Nicholas, W. J. Jenkins, and W. L. Marsh. *British Medical Journal* [*Brit. med. J.*] **1**, 1458–1460, June 22, 1957. 1 fig., 8 refs.

The propositus of this study was a married woman aged 29 years who attended the Essex County Hospital, Colchester, for antenatal blood grouping. On investigation she was found to have erythrocytes of two distinct groups, proportions being 49% in the O series, and 51% in the A_1 series, one being " inherited " and one " foreign ". She had a twin brother who had previously been shown to be a blood chimera, with inherited and foreign components in the proportions of 61% A_1 series and 39% O series. Blood typing for the ABO, MNSs, P, Rh, Luther, Kell, Lewis, Duffy, and Kidd systems was carried out on the twins and on the parents, husband, and children of the propositus, and the results, including those for each component of the twins' blood, are given. Apart from the twins no abnormalities were noted and it seems certain that the mixture in such twins arises from an exchange of erythroblasts *in utero*.

The two components of the twins' blood differed in the ABO, MNSs, and Rh systems, but although the two inherited components were different in the Lewis system Le(a−b+) for the female and Le(a+b−) for the male, the foreign component was the same as the inherited in each of the pair. As salivary secretion tests supported the Le^a typing the authors conclude that this observation supports the contention of other workers that the Lewis antigen belongs to the tissues and is only secondarily attached to the erythrocytes.

Nuclear sexing of the neutrophil granulocytes revealed foreign leucocytes in the blood of the male twin. This was probably the case also in the female, and the authors suggest " blood chimera " rather than " blood group chimera " as the more accurate description of such persons. *E. A. Cheeseman*

1029. **Combinations of Hemoglobin G, Hemoglobin S and Thalassemia Occurring in One Family**
H. C. Schwartz, T. H. Spaet, W. W. Zuelzer, J. V. Neel, A. R. Robinson, and S. F. Kaufman. *Blood* [*Blood*] **12**, 238–250, March, 1957. 3 figs., 18 refs.

The occurrence of three abnormalities of haemoglobin synthesis in a single family made it possible to observe their segregation and to obtain information as to whether or not the genes were alleles. The abnormalities were sickling, thalassaemia, and the presence of a rare haemoglobin named by the authors haemoglobin G. (This haemoglobin was not really identical with the haemoglobin G reported by Edington and Lehmann (*Lancet*, 1954, **2**, 173), but resembled it very closely.) All the three abnormal genes were inherited independently, and their products were therefore not allelomorphs. This was already known to be so for the genes of thalassaemia and of haemoglobins A and S (which are allelomorphs), but the only haemoglobin so far known not to be an allelomorph of all the others was haemoglobin F (foetal haemoglobin). The " haemoglobin G " described in this present investigation is therefore the first adult haemoglobin which logically ought to be regarded as a normal variant of haemoglobin rather than as an abnormal variant. *H. Lehmann*

1030. **Familial Hypertrophic Polyneuritis. Review of a Previously Reported Family**
P. B. Croft and N. H. Wadia. *Neurology* [*Neurology*] **7**, 356–366, May, 1957. 5 figs., 28 refs.

1031. **Hereditary Pancreatitis: Report on Two Additional Families**
J. B. Gross and M. W. Comfort. *Gastroenterology* [*Gastroenterology*] **32**, 829–854, May, 1957. 9 figs., 11 refs.

Public Health and Industrial Medicine

1032. **An Association between Social Circumstances and Appendicitis in Young People**
J. A. H. Lee. *British Medical Journal* [*Brit. med. J.*] 1, 1217–1219, May 25, 1957. 22 refs.

In this paper from the Social Medicine Research Unit of the Medical Research Council, London Hospital, a comparative study is presented of the incidence of appendicectomy in 6,771 men examined at various centres in England in 1953–4 before call-up for national service. It was found that the operation had been performed on over 6% of those coming from grammar and independent schools, compared with 3·4% of those from secondary modern schools. In Scotland the incidence was consistently highest in the Clydeside and West of Scotland districts, reaching 7·2% in some places. These variations in the geographical distribution of the operation in young men were not closely reflected in the total death rates from appendicitis at all ages. There was, however, a definite excess in Glasgow of deaths from appendicitis in the younger age groups; a similar excess death rate was found among boys under 15 in the rest of Scotland and also in Wales.

The author discusses the possible reasons for these phenomena, and concludes that uncertainty about the aetiology of appendicitis and local differences in methods of diagnosis and treatment do not permit any firm conclusions to be drawn, except that there would appear to be a link between appendicitis and duodenal ulcer, similar variations having been noted in the incidence and distribution of the latter disease. Finally he points out that there are a number of unknown factors concerning appendicitis—multiple social ones—which call for much closer study. [A very interesting, concise, and lucid paper.] *R. J. Matthews*

1033. **Survival of Variola Virus in Raw Cotton**
F. O. MacCallum and J. R. McDonald. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **16**, 247–254, 1957. 6 refs.

For many years imported raw cotton has been suspected on epidemiological grounds as a vehicle for the introduction of variola virus into Great Britain. Since the potential risk to workers in cotton mills is probably greatest in the earliest stages of manufacture, and as the possibility of infection will continue until sanitary conditions in the cotton-producing areas of the world improve, laboratory experiments were undertaken at the Virus Reference Laboratory, London, to determine the duration of survival of the virus in raw cotton.

In these studies variola virus contained in scabs from a smallpox patient was enclosed in samples of raw cotton, suspended over saturated solutions of various salts in wide-necked screw-capped jars, and incubated at 30° C. at relative humidities (R.H.) of 58, 73, and 84%. As a control, other scabs were placed in small screw-capped bottles kept at laboratory temperature and humidity (20 to 24° C. and R.H. 55 to 75) and exposed to diffuse daylight. It was found that viable variola virus persisted in this control material for at least 18 months, whereas in the test material under these experimental conditions no virus was detected after 3 months at R.H. 73 and 84, or after 6 months at R.H. 58. In a second experiment no virus was isolated after 70 days at R.H. 58, after 112 days at R.H. 73, or after 60 days at R.H. 84. It is therefore considered, on the basis of the quantities of virus surviving under the various conditions, that there would be little danger from variola virus if cotton were stored before shipment for at least 6 months at the temperatures (30° to 40° C.) and humidity prevailing in cotton-growing areas where smallpox is endemic. *J. E. M. Whitehead*

1034. **Epidemic of Meningoencephalitis and Bornholm Disease**
H. G. Langdale-Smith, D. M. Langdale-Smith, and B. R. Wilkinson. *British Medical Journal* [*Brit. med. J.*] **1**, 805–807, April 6, 1957. 2 figs., 5 refs.

The relationship between meningitis and Bornholm disease has already been discussed by several workers, while a Swedish group of investigators has described an outbreak of Bornholm disease with a high incidence of aseptic meningitis.

The present authors now report a clinical study of a localized epidemic of meningoencephalitis and Bornholm disease which occurred in the small hamlets of Stretton Grandison (population 550) and Eggleton (population 133), Herefordshire, during the latter part of the summer of 1956. The cases occurring in August and September were of Bornholm disease; at the end of September these cases " merged into an outbreak of meningo-encephalitis ", centred largely on Stretton Grandison school. At the end of October cases of encephalitis became fewer and Bornholm disease reappeared; meanwhile there were a few cases of an intermediate type.

In the cases of Bornholm disease (17) the onset was sudden, with acute abdominal and thoracic pain and great prostration. The infection lasted 2 to 10 days, as did the incubation period. In the cases of meningoencephalitis (27) the onset was slow or sudden, with severe frontal headache, pyrexia, vomiting, neck stiffness, and photophobia. The intermediate cases (8), which occurred in houses where there was already one type of case, were characterized by headache and vomiting, but no photophobia or neck stiffness. The incidence increased until the end of September and early October, when the peak was reached. Altogether there were 52 cases, 25 of which occurred at the school of 47 children. The infection seemed to have spread by direct contact (finger–mouth route). There was no evidence of

food contamination. Where there was contact with massive infection, as in school, a large proportion of subjects contracted the disease, whereas in the houses the attack rate depended on susceptibility (all 5 occupants in one house, but only one out of 14 in another). None of the children in the school had been vaccinated against poliomyelitis. *F. T. H. Wood*

1035. **Newborn Pneumonitis Virus (Type Sendai). Evidence of Infection in South-west Scotland**
R. G. SOMMERVILLE. *British Medical Journal* [*Brit. med. J.*] **1**, 1145–1148, May 18, 1957. 5 refs.

Paired sera taken in the acute and convalescent stages from adults and infants with respiratory tract infections, including pneumonia, at Ruchill Hospital, Glasgow, were examined for Sendai virus by complement-fixation and haemagglutination-inhibition tests. The author refers to this virus, which was first isolated in Japan from newborn infants with pneumonia, as the "newborn pneumonitis virus, type Sendai". Out of 444 paired sera, 9 (2%) showed a significant fourfold rise in titre of complement-fixing antibodies, and of these 9 pairs, 4 also showed a fourfold rise in haemagglutination-inhibiting antibodies. In general, antibody appeared between the 5th and 10th days of illness, reaching a peak at the end of the second or third week. The clinical features of the illnesses were indistinguishable from influenza (5 cases) or pneumonia (4 cases).

[Despite its original isolation from the newborn and the nomenclature adopted by the author, no evidence of recent infection was obtained in 72 paired samples of serum from infants. The 9 instances of Sendai infection reported here occurred in patients aged between 35 and 75.] *D. Geraint James*

INDUSTRIAL MEDICINE

1036. **Twenty-five Years of Silicosis. Analysis of Material from the Swiss Accident Insurance Fund, January 1, 1932, to December 31, 1956.** (25 Jahre Silikose. Das Krankengut der Schweizerischen Unfallversicherungsanstalt vom 1. Januar 1932 bis 31. Dezember 1956)
R. LECHMANN. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **87**, 528–535, May 4, 1957. 5 figs.

The author presents a detailed review of all the cases of silicosis notified between 1932 and 1956 to the Swiss Insurance Fund, together with numerous tables and several graphs and histograms. During the 25-year period 6,275 cases of silicosis were notified, but only 3,908 of these were accepted, 1,668 being rejected on medical grounds and 675 on legal grounds, principally because the disease was held to have been contracted outside Switzerland.

Of the 3,908 accepted cases, 53% were in miners or tunnellers, 25% in quarrymen, and 20% in workers in various metal industries. One of the histograms shows first a steadily rising number of cases of silicosis especially among miners during 1932–44, a sudden sharp rise in 1945, fluctuation till 1949, a relatively stationary period for 5 years, and finally another sharp rise in 1956, mostly among quarrymen.

In regard to the individual groups of workmen, the author considers that among miners the disease will occur less frequently in the future and its course will be less severe. He comments on the former danger to sandblasters, in whom the disease used to progress rapidly, invalidity occurred early, and death ensued after a much shorter period of exposure than in other occupations. In this occupation, however, conditions have been so much improved that now these workers can be regarded as being the best protected in the whole metal industry. Women are only mentioned in relation to the polishing industry, in which during the 25-year period 10 men and 6 women were affected.

Another graph shows that in only about 50% of the cases notified were the patients receiving any compensation at all, though this was to be expected later in view of the nature of the disease. During the two 5-year periods 1947–51 and 1952–6 the diagnosis of silicosis was wrong in 22% of cases, a margin of error now the subject of investigation. There were 13 cases of suicide in which the disease was held to be either wholly or partly responsible, contributory causes being fear of a painful end, knowledge of the progressive nature of the disease, and anxiety for dependants.

Preventive measures, such as spraying of work faces, dust extraction apparatus, use of helmets supplied with fresh air, preliminary radiological and clinical examination before entering the industry, and subsequent *x*-ray examination at regular intervals are mentioned. Finally, a map shows the geographical distribution of the disease throughout Switzerland.

[In view of the numbers of cases occurring especially among miners and quarry-workers it is regrettable that the total number of workers for the various industries, in quinquennia, are not given. This might have made the effects of the preventive measures more evident.] *W. K. Dunscombe*

1037. **Silicosis Hazards in Enamelling. A Medical, Technical, and Experimental Study**
L. FRIBERG and H. ÖHMAN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 85–91, April, 1957. 4 figs., 7 refs.

The occurrence of silicosis in enamel workers has been described by several authors since 1940. The present study, reported from the Karolinska Institute of Hygiene, Stockholm, was carried out at an enamelling works in Sweden. The various processes employed in enamelling are described. Siliceous materials used in the making of enamel include quartz and quartz felspar which, with other ingredients, are fused and ground. Metal articles are coated with the enamel by dipping or, recently, more often by spraying.

In all, 35 workers were studied, among whom 6 cases of silicosis were diagnosed and 2 more suspected. Disability (assessed at $33\frac{1}{3}$, 20, and 15% respectively by an insurance board) was present in 3 of the cases. The known minimum duration of exposure before appearance of silicosis was 9 years, but was probably in fact much

longer. Tuberculosis was not detected in any of the cases.

In various technical studies the efficiency of ventilation of spraying booths was assessed and in dust samples collected with a midget impinger the quartz content was estimated by *x*-ray diffraction of particles smaller than 5μ. It was found that the spraying of inner surfaces of articles being enamelled produced higher particle counts than the spraying of external surfaces, the enamel aerosol having apparently a greater tendency to rebound from them. Work at the firing ovens was also dusty, the analysis of airborne and of deposited dusts at this site showing a high quartz content.

In animal experiments involving the intraperitoneal injection of enamel powders into rats it was shown that of the enamels in use at this works, two produced a typical silicotic fibrosis similar to that produced by a control injection of pure quartz. *L. W. Hale*

1038. **Radiological Surveys of Working Quarrymen and Quarrying Communities in Caernarvonshire**
T. F. JARMAN, J. G. JONES, J. H. PHILLIPS, and H. E. SEINGRY. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 95–104, April, 1957. 5 figs., 19 refs.

The authors describe a radiological survey which was undertaken by the Welsh Regional Hospital Board in an attempt to determine (1) the prevalence of pneumoconiosis and of active pulmonary tuberculosis among slate-quarry workers; and (2) the prevalence of tuberculosis among past and present slate-quarry workers and, for purposes of comparison, that among other male workers not concerned with quarrying among the same population. In all, workers at five slate quarries and in three rural communities were studied. The films were read independently by three observers. Cases of suspected pulmonary tuberculosis were observed for one year or more at the Bangor Area Chest Clinic, and classified as " active " or " active and infectious " according to the bacteriological and radiological findings over that period. By various means of persuasion, which are described, no fewer than 2,432 quarrymen (90% of the workers) were examined by radiography. Among these, 203 cases of pneumoconiosis of Category 2 or higher, including 15 cases of progressive massive fibrosis, were found, while 27 of the men with " suspected tuberculosis " were considered after follow-up to be suffering from active tuberculosis, 13 of them being sputum-positive for tubercle bacilli.

It is noted that the prevalence of pneumoconiosis in these workers is much lower than that among past and present coal-miners in the Rhondda Fach, the figures being 83·5 per 1,000 quarrymen and 300 per 1,000 miners in the Rhondda when Categories 2 and 3 only were compared. A comparison of the prevalence of infectious tuberculosis among working quarrymen with that among surface and underground workers at the Rhondda collieries showed a figure of 5·3 per 1,000 quarrymen compared with 1·4 per 1,000 coal-mine workers. The incidence of tuberculosis among quarrymen is higher than that in any other industry surveyed by the Welsh Mass Radiography Service.

In the " total community " survey of three rural communities, 75% of the population were *x*-rayed. Of 618 quarry and ex-quarry workers, 37 had active pulmonary tuberculosis (11 being infectious), which is equivalent to a rate of 60 active cases per 1,000, compared with 7·5 per 1,000 in the Rhondda study. Among males not working in quarries the rate was 46·4 active cases per 1,000 (Rhondda 13·5 per 1,000). Among females over 15 a similar trend was found. *L. W. Hale*

1039. **An Outbreak of Tri-*ortho*cresyl Phosphate (TOCP) Poisoning in Durban**
M. SUSSER and Z. STEIN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 111–120, April, 1957. 3 figs., 21 refs.

The authors recount the circumstances of 8 previously recorded outbreaks of tri-*ortho*cresyl phosphate (TOCP) poisoning, from the first in 1899 to the last in 1946, and describe an outbreak in Durban, South Africa, in 1955, involving 11 Africans aged 7 to 46 years. The TOCP is thought to have been absorbed from drinking water stored in drums which had previously contained this compound. There was, however, no proof of this; the use of TOCP in cooking was not definitely excluded, and it was known that this compound was used extensively and under adverse conditions in a nearby paint factory.

The clinical features of this intoxication were distinctive. Some 14 to 28 days after the poison had been ingested there were sharp cramping pains in the calves with numbness and tingling of the feet. Weakness followed in a day or two, and the patient was often unable to keep his balance, an abrupt fall to the ground being the first symptom in some patients. A picture of peripheral neuritis developed, with loss of ankle-jerks and impaired sensation. Similar changes later affected the upper limbs, leading to wasting of the hand muscles and wrist-drop. Upper neurone symptoms were seen soon after, characterized by exaggerated knee-jerks.

The authors describe two features not previously reported: (1) the appearance of upper neurone lesions during the first month of the illness, and (2) enlargement of the parotid gland, which was attributed to the action of the poison on a gland that was already affected by malnutrition.

The course of the disease varied. All patients were still affected when last seen 5 months after the onset of symptoms, although most of them had started to improve. The authors were able to study the present condition of 4 patients who had been affected in an outbreak in Durban in 1938. All showed some signs of the disease (18 years afterwards), the most severely affected still suffering from a spastic gait and foot-drop.

R. E. Lane

1040. **Manufacture of Tricresyl Phosphate and Other Alkyl Phenyl Phosphates: an Industrial Hygiene Study. 1. Environmental Factors**
I. R. TABERSHAW, M. KLEINFELD, and B. FEINER. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **15**, 537–540, June, 1957. 2 refs.

x*

Forensic Medicine and Toxicology

1041. **The Relationship between the Demonstrability of Sex Chromatin in the Epidermal Cells of the Cadaver and the Interval since Death.** (Bezeihungen zwischen der Nachweisbarkeit des Geschlechtschromatins in den Oberhautzellen und dem Leichenalter)
F. SCHLEYER. *Schweizerische Zeitschrift für allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path. Bakt.*] **20**, 280–286, 1957. 21 refs.

In this communication from the Institute of Forensic Medicine, University of Bonn, the author first describes the location, shape, and staining properties of sex chromatin, which in his experience is best differentiated by the Feulgen staining reaction. In fresh preparations detailed examination of the preparation is not necessary, mere scanning being sufficient to distinguish male and female epidermis. Sex chromatin in the skin remains unchanged post mortem for at least 3 days. Experiments are then described in which from each of 3 female cadavers a foot was amputated and retained at room temperature, samples of skin being then taken twice from each foot while decomposition proceeded and examined for sex chromatin. Only definitely positive and definitely negative nuclei were counted.

As decomposition proceeded it was found that " female " sex chromatin became " male " (by the 11th day in one case). The still detectable chromatin masses were more indistinct than in fresh preparations, so that obviously the accuracy of diagnosis of sex post mortem is related to the conditions under which the corpse has been kept. The author concludes that in circumstances favouring slow decomposition differentiation of sex is possible for up to one week, but if decomposition of the skin is already evident and if on examination the sex chromatin appears to be " male " no certain diagnosis of sex is possible. On the other hand the sex can be regarded as female, regardless of the period which has elapsed since death, if at least 25% of the nuclei are chromatin-positive. It is necessary, however, to examine several hundred nuclei, in several preparations from different parts of the skin, since the frequency or the demonstrability of sex chromatin fluctuates considerably from preparation to preparation.

W. K. Dunscombe

1042. **The Treatment of Lithium Poisoning**
D. A. COATS, E. M. TRAUTNER, and S. GERSHON. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **6**, 11–15, Feb., 1957. 7 refs.

The authors report from the University of Melbourne that during the treatment with lithium salts of 300 psychotic patients minor degrees of poisoning were encountered and treated merely by withholding the drug for several days, this being combined in some cases with oral administration 3 times a day of 1 g. of potassium chloride. In severe cases treatment was directed particularly to the rapid reduction of the large intracellular fraction. As soon as the earliest symptoms of lithium poisoning appeared—anorexia, loss of weight, nausea, muscular fasciculations, and ataxia—administration of lithium was stopped and a high fluid intake maintained. Cellular uptake of potassium was encouraged by oral or intravenous administration of potassium. Established lithium poisoning is associated with starvation ketosis, and the authors consider it essential to correct this by administration of not less than 200 g. of glucose in 24 hours, accompanied simultaneously by doses of insulin. This treatment serves also to promote the cellular uptake of potassium and the release of cellular lithium. In severe cases of acidosis it may be necessary to give an intravenous infusion of sodium bicarbonate solution. Six cases are described in which these principles of treatment were applied. *Norval Taylor*

1043. **Barbiturate Poisoning Treated by Physiological Methods with Observations on Effects of *beta*, *beta*-Methylethylglutarimide and Electrical Stimulation**
F. PLUM and A. G. SWANSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 827–835, March 9, 1957. 3 figs., 17 refs.

Noting the lack of unanimity regarding the most effective treatment of barbiturate poisoning, the authors review the treatment of 243 such patients admitted to King County Hospital (University of Washington), Seattle, over a period of 3¼ years. Since 160 of these patients were comatose on admission the chief danger was respiratory obstruction, so after the respiratory passages had been cleared the airway was maintained by suction and respiration maintained by means of a mechanical respirator if necessary. In 141 of the cases the stomach was washed out. Saline infusions were given and, if the blood pressure was 85 mm. Hg or less, ephedrine or methoxamine was also given. Cases of dangerously low blood pressure were treated with phenylephrine or noradrenaline. In patients given oxygen the alveolar CO_2 tension was frequently determined to avoid accumulation of carbon dioxide resulting from depressed ventilation. Of 5 patients given $\beta\beta$-methylethylglutarimide, 4 showed increased reflexes but in the 5th the effects were slight; all required other treatment in addition. Electrical stimulation was tried in 10 patients; this tended to increase ventilation and so to hasten recovery, but was not by itself a sufficient treatment, the effects being much the same as those of other painful stimuli. *V. J. Woolley*

1044. **Salicylate Intoxication Treated with Intermittent Positive-pressure Respiration**
S. FREIER, B. W. NEAL, H. I. A. NISBET, G. J. REES, and F. WILSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1333–1335, June 8, 1957. 14 refs.

Anaesthetics

1045. **Alphaprodine (Nisentil) Hydrochloride in Anesthesia. Its Use, with or without Antagonists, for Supplementation or as Sole Agent**

H. I. LIPSON and H. R. BRADFORD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1244–1248, April 6, 1957. 10 refs.

Narcotic analgesics were used as the main agents in an anaesthetic sequence, with the appropriate antagonists to prevent undue respiratory depression, in a series of 224 patients undergoing operation at the Veterans Administration Hospital, Brooklyn, N.Y. In all except 15 of the patients the analgesic was alphaprodine and the antagonist was levallorphan administered in a ratio of 1:50 or 1:100. In most cases anaesthesia was with thiopentone, nitrous oxide, cyclopropane, and local and regional blocks, but in 84 patients alphaprodine was the sole analgesic and in some of these nalorphine was the antagonist. From the results the authors consider that alphaprodine can be given in massive doses (up to 1,600 mg.) and still allow adequate spontaneous respiration, provided an appropriate antagonist is given concurrently. An initial respiratory depression in a few instances was of short duration. In a small group of cases in which alphaprodine was the only analgesic it was possible to perform a major operation with the patient conscious, endotracheal intubation being carried out and tubocurarine given as a relaxant. The authors state that levallorphan selectively antagonizes the respiratory depression and does not inhibit the analgesia. *Donald V. Bateman*

1046. **Buthalitone Sodium in Out-patient Anaesthesia**

A. G. HENDERSON and J. MACKETT. *British Medical Journal* [*Brit. med. J.*] **1**, 1095–1097, May 11, 1957. 8 refs.

Buthalitone sodium, first described by Miller in 1936 (*J. Amer. chem. Soc.*, **58**, 1090), is a thiobarbiturate, and like other thiobarbiturates is a yellow powder very soluble in water. The solution, however, is easily decomposed by atmospheric carbon dioxide, and sodium carbonate is added to prevent this. At Luton and Dunstable Hospital, Luton, a total of 200 out-patients, aged 6 to 82 years, were anaesthetized with this drug combined with nitrous oxide and oxygen, the duration of anaesthesia varying from 5½ to 40 minutes, average 7 minutes. Atropine was given preoperatively, followed half an hour later by a single induction dose of 11 mg. of buthalitone per kg. body weight; in this dosage the drug did not cause respiratory depression. Anaesthesia was continued with nitrous oxide 80% and oxygen 20%. Patients were awake within 3 minutes, were able to sit up within 4 minutes, and ready to go home within 20 minutes of the cessation of anaesthesia. In children the dose was reduced to 8 mg. per kg. body weight. The authors state that induction is smooth, operating conditions are satisfactory, and recovery is rapid, making this form of anaesthesia very suitable for out-patients. In 25 cases in which intubation was required injection of buthalitone was followed immediately by administration of 50 mg. of suxamethonium chloride; maintenance was with nitrous oxide, oxygen, and trichlorethylene.

W. Stanley Sykes

1047. **Cardiovascular Function in Hypothermic Anesthetized Man**

J. C. ROSE, T. F. MCDERMOTT, L. S. LILIENFIELD, F. A. PORFIDO, and R. T. KELLEY. *Circulation* [*Circulation (N.Y.)*] **15**, 512–517, April, 1957. 3 figs., 19 refs.

Being doubtful about the application to man of the experimental findings observed during hypothermia induced in dogs, the authors, working at Georgetown University Medical Center, Washington, D.C., have made detailed observations on the cardiovascular changes in 10 patients immediately before and after induction of hypothermia. None of the patients had pre-existing cardiovascular disease and they were undergoing surgery for a variety of conditions. After induction of anaesthesia but before cooling was begun the electrocardiogram, femoral blood pressure from an intra-arterial needle, and blood volume and circulation times (using radioactive tracer techniques) were recorded. From these data were calculated the peripheral resistance and cardiac output. Similar readings were then obtained after artificial cooling but before any surgical intervention or intravenous transfusion. Cooling was by ice-packs, shivering being controlled by anaesthetic agents which usually included ether or cyclopropane but not chlorpromazine or relaxants. Rectal temperature was recorded and cooling was discontinued when this reached 31° to 32·5° C.

The results showed that the heart rate was consistently slowed and the pressure-pulse contour showed a consistent change in pattern. Other parameters varied inconsistently—blood pressure, for instance, tended to rise but subsequently fell when surgery was begun. Increased cardiac work associated with systemic vasoconstriction during cooling (which occurred in 5 of the 10 patients) led the authors to question the advisability of hypothermia for " poor-risk " candidates for cardiac surgery, but they suggest that the use of autonomic blocking agents may reduce this risk by diminishing the intensity of the vasoconstrictor response to cold.

They stress the difference between the carefully controlled environment of experiments on laboratory animals and the relatively uncontrolled environment of the operating theatre with its clinical limitations, and suggest that the technique of hypothermia should be used most cautiously until further information is available, especially in regard to total and regional oxygen consumption, regional blood flow, and other chemical and metabolic changes in the hypothermic patient.

Donald V. Bateman

Radiology

EXPERIMENTAL

1048. **Experimental Micro-lymphangiography.** [In English]
S. BELLMAN and B. ODÉN. *Acta Radiologica* [*Acta radiol. (Stockh.)*] **47**, 289–307, April, 1957. 9 figs., 42 refs.

This paper describes a technique of microlymphangiography developed by the authors in a number of experiments carried out at the Karolinska Institute and Serafimerlasarettet, Stockholm. Mature rabbits were used, mostly living and under anaesthesia, but in some cases recently killed. In most experiments the contrast medium used was "thorotrast" or "umbradil" (diodone) 25%, and was injected through a fine needle into the subcutaneous tissue of the leg or the lobe of the ear. Serial radiographs were taken at short intervals starting about 10 seconds after beginning the injection, the resulting films being magnified to varying degrees depending upon the nature of the part injected and the photographic material used. Studies were made of the quality of microlymphangiograms obtained at kilovoltages which ranged from 20 to 50, and the authors give a detailed account of the theoretical aspects of the absorption of *x* rays by varying types and concentrations of a number of different opaque media.

The films demonstrated an immediate filling of lymphatic channels radiating from the pool of opaque medium and relatively remote from it, and from this fact the authors conclude that some of the medium was injected directly into the lymph vessels. In some cases an increase in density occurred about 3 minutes after injection, suggesting subsequent absorption into the ducts by other routes. With thorotrast the density of the medium remained fairly constant in the lymph vessels for about 8 or 9 minutes and thereafter diminished, with complete disappearance of the medium after 45 minutes. Diodone gave comparable results in the first few minutes after injection, but disappeared more rapidly, usually within 10 minutes. In the ear the contrast medium usually appeared in lymph vessels in the zone between the site of injection and the middle branch of the posterior auricular artery, and the rich network of lymph vessels around this artery and occasionally around smaller arteries and veins was visualized. When the injection was made near the edge of the ear the lymph flow sometimes followed the margin, but the medium never spread over a large area.

The authors found that the use of diodone was sometimes accompanied by inflammatory reactions in the tissues, but this did not occur with thorotrast. The latter medium is therefore to be preferred in experimental animals, to which the disadvantages attending its use in man do not apply.

A number of microlymphangiograms are reproduced.
A. M. Rackow

RADIODIAGNOSIS

1049. **Intracranial Calcification.** (Les calcifications intracraniennes)
J. E. PAILLAS, J. LEGRÉ, and A. MASSAD. *Presse médicale* [*Presse méd.*] **65**, 768–771, April 24, 1957. 11 figs.

Intracranial calcification was formerly thought to be rare, but owing to recent improvements in neuroradiological technique it is now found to be relatively frequent and is an important factor in arriving at an accurate neurological or neurosurgical diagnosis. In this paper from the Hôpital de la Timone, Marseilles, the authors summarize their analysis of two consecutive series of radiographic examinations, each embracing 1,000 cases, in the first of which older radiological techniques were employed while in the second series films taken with more recent apparatus, such as a rotating anode and fine-grain intensifying screens, were used, as well as such procedures as tomography, angiography, and pneumoencephalography. In the first series there were 388 cases showing intracranial calcification and in the second 426 cases, the increased incidence being attributed mainly to the improved techniques. Of the 814 cases, the intracranial calcification, for the most part of the pineal gland, was considered to be "physiological" in 655 and pathological in 159, the respective proportions being thus about 32% and 8%.

"Physiological" calcification was found chiefly in the meninges, including the tentorium, the clinoid ligaments, the pineal gland, the choroid plexuses, and the Pacchionian bodies. Pathological calcification occurred in association with vascular abnormalities such as atheroma of the internal carotid artery, basal aneurysms, angiomatous malformations, subdural haematoma, intracerebral haematoma, cerebral endarteritis, Fahr's disease, and infantile cerebral atrophy following anoxia. Pathological calcification was also seen in cases of phakomatosis, tuberous sclerosis, neuroangiomatosis of the Sturge–Weber type, and in neurofibromatosis of the von Recklinghausen type. The calcification found in various types of intracranial tumour, certain infections, parasitic conditions, tuberculoma, toxoplasmosis, and old cerebral abscesses is briefly considered. The diagnostic significance of the various types and sites of calcification is discussed. *J. MacD. Holmes*

1050. **Follow-up Study of 844 Neoplasm Suspects Identified in a Mass Chest *X*-ray Survey**
C. D. MCCLURE. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **72**, 307–316, April, 1957. 1 fig., 7 refs.

On the basis of the findings of a mass chest radiography survey in Pittsburgh and Allegheny County, Pennsylvania, 844 subjects suspected of having a neoplasm were followed up for 30 months to determine the

clinical diagnosis and the subsequent mortality. At the initial examination of 800,000 subjects 70-mm. postero-anterior chest radiographs were taken; later, all patients with suspected abnormalities were recalled and 14 × 17-cm. postero-anterior radiographs were obtained, with lateral or oblique views if requested. The survey was limited to patients over 15 years of age.

There were wide variations between the readings of the small and large radiographs. It was not established that the large radiographs were better than the small ones for detecting the presence of a neoplasm. Of the 844 patients, 5·5% were found to have primary malignant lung tumours, 3·2% metastatic malignancy, 27·6% benign neoplasms, and 15% pulmonary tuberculosis. The difficulty of accurately distinguishing on radiographs between lung tumours, tuberculosis, and other lung diseases is reflected in the fact that among those suspected of lung tumour the percentage with a clinical diagnosis of lung tumour was no higher than the percentage with clinical diagnosis of tuberculosis or other chest diseases. Of the 46 patients with primary cancer of the lung, 28 had died within 12 months of the end of the survey and 31 had died within 30 months. In 8 of the 15 survivors the diagnosis was confirmed microscopically and pneumonectomy was performed; in 7 the diagnosis was based on the radiological findings alone. Deaths due to primary lung cancer occurred among patients in other diagnostic categories, but somewhat later than the deaths in the lung cancer group. In most of these, presumably misdiagnosed, cases the initial lesion was small or not well defined.

John H. L. Conway-Hughes

1051. **Bronchospasm in Bronchography**
T. H. HEWLETT, A. J. PUGLISI, and W. F. BOWERS. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 609–616, May, 1957. 2 figs.

Bronchospasm was encountered during bronchography in 7 out of a series of 79 bronchographic studies carried out at the Brooke Army Hospital, Fort Sam Houston, Texas. Of the 7 patients, 3 were asthmatic; 4 had no history of asthma. The authors point out that bronchospasm produces slight cylindrical dilatation of the main bronchi; there is a decrease in or complete absence of filling of the smaller bronchi and alveoli. The appearance simulates that of mild bronchiectasis, but is transient; in a repeat examination the findings are usually normal.

D. E. Fletcher

1052. **The Sialographic Differentiation of Mikulicz's Disease and Mikulicz's Syndrome**
P. RUBIN and B. E. BESSE. *Radiology* [*Radiology*] **68**, 477–487, April, 1957. 6 figs., bibliography.

More than 100 sialographic studies carried out on 43 patients led to the diagnosis in 14 cases of Mikulicz's syndrome (enlargement of the parotid gland secondary to enlarged lymph nodes, due in 3 cases to leukaemia, in 5 to sarcoidosis, in 5 to lymphoma, and in one to tuberculosis). In the remaining 29 cases the diagnosis was of Mikulicz's disease.

In most cases of Mikulicz's syndrome the architecture of the gland remains intact and a normal branching duct system, possibly with lateral displacement, is seen in the early to moderately advanced stages; reflex stimulation of the gland leads to complete evacuation. In the later stages, when invasion occurs, the injection of small amounts of contrast medium often causes pain, showing that the capacity of the duct system has been reached; in such cases there is a striking decrease in arborization, but it remains exceptional for the medium to be retained after stimulation.

In contrast, in Mikulicz's disease the earliest stage is marked by narrowing of the interlobular ducts by periductal lymphocytic infiltration and septal fibrosis. Functional glandular tissue continues to secrete against the resistance of the narrowed duct system, resulting in diffuse, punctate dilatation of the peripheral ducts, which may be less than 1 mm. in diameter, and retention of the medium after stimulation. In the next stage the globules of retained contrast material in the intralobular ducts increase in diameter to 1 or 2 mm. and contrast with the scarcity of ducts in the interlobular septa. In the third stage the globules coalesce, become irregular in size and distribution, and decrease in number. Finally, with destruction of the duct system, there is a bizarre pattern which can be differentiated from neoplastic disease by the presence of multiglandular spread.

Denys Jennings

1053. **Meconium Ileus**
R. E. HERSON. *Radiology* [*Radiology*] **68**, 568–571, April, 1957. 2 figs., 5 refs.

The authors have reviewed 18 cases of meconium ileus, proved at operation or necropsy, which occurred between 1945 and 1955 at the Babies Hospital, New York. In 17 cases *x*-ray films were available. They conclude that colonic gas should be demonstrable in such cases within 12 hours of birth, but individual variation makes the diagnosis of obstruction hazardous before 24 hours unless failure of the gas shadows to progress is seen on successive films. Abdominal calcification is good evidence of peritonitis. Fluid levels were present in 5 of the 8 complicated cases and in 5 of the 7 uncomplicated cases in which the patient was examined in the erect position. Absence of fluid levels is therefore not a reliable sign of meconium ileus. Air bubbles coinciding with a palpable mass were present in 12 cases and, though not specific, were the most helpful sign. So far 14 of the patients have died—11 on the first admission, another from respiratory infection at 2 months, and 2 from congenital fibrosis of the pancreas at 2 years and 3¾ years respectively.

Denys Jennings

1054. **The Intravenous Cholangiographic Diagnosis of Partial Obstruction of the Common Bile Duct**
R. E. WISE, D. O. JOHNSTON, and F. A. SALZMAN. *Radiology* [*Radiology*] **68**, 507–525, April, 1957. 13 figs., 21 refs.

In this paper from the Lahey Clinic and the New England Baptist Hospital, Boston, the authors analyse their experience of intravenous cholangiography in the diagnosis of partial obstruction of the common bile duct. The injection of 20 ml. of 52% "cholografin"

methylglucamine opacified the bile ducts in 228 out of 256 patients suspected of gall-bladder disease. In 96 cases in which the cholangiogram was normal and disease of the gall-bladder was considered to be excluded the diameter of the common duct ranged from 2 to 14 mm., with a mean of 5·5 mm. [S.D. not given]; 9 of these patients were operated on and in 8 the common duct was explored, but no abnormality was found. In the 82 cases in which there was no gall-bladder shadow the diameter of the common duct ranged from 3 to 22 mm., with a mean of 9·3 mm.; and in the 45 cases with stones or with a poor gall-bladder shadow the diameter ranged from 3 to 17 mm., with a mean of 8·3 mm. In 64 cases in the last two groups in which gall-bladder disease was proved surgically the average diameter of the common duct was 9 mm., being 13·1 mm. in the 21 with calculi of the duct and 6·6 mm. in the 43 without calculi. The critical diameter of the duct was about 10 mm., only 3 of the 21 ducts containing stones being narrower than this and only 7 of the 43 ducts without stones being wider.

In a second group of observations 512 injections of cholografin were given to 490 patients who had undergone cholecystectomy at some time in the previous 30 years. In 397 cases the diameter of the common duct was measurable and ranged from 3 to 30 mm., with a mean of 9·1 mm.; this may be compared with the mean diameter of 9 mm. found before cholecystectomy in the group of 64 cases mentioned above. The diameter of the duct alone was not a useful indicator of obstruction. In the 6·5% of cases in which the diameter was over 15 mm. obstruction was always present, while there was no case of obstruction among the 8% in which the diameter was less than 5 mm.; but in 84·5% of the cases the diameter fell in the intervening range and was of no diagnostic value. There was no relation between the diameter of the duct and the time interval since cholecystectomy, so that the old idea of a compensatory dilatation would seem to be unfounded. In 31 cases the presence of calculi in the common duct was proved surgically. The calculi had been visualized before operation in 10 of the 17 cases in which they were the sole cause of obstruction and in 8 of the 14 in which obstruction was associated with a stricture; in 12 of the remaining 13 cases in which the calculi were not visualized the presence of obstruction had been diagnosed correctly from the persistent density of the duct shadow 60 to 120 minutes after the injection of cholografin (in contrast with the decrease in density which normally begins after about 50 minutes). In a further 16 cases obstruction due to fibrosis of the sphincter of Oddi or ampulla of Vater, without associated calculi, was demonstrated at operation; in 14 of these the obstruction had been correctly predicted from the cholangiograms, as also in all of 11 similar cases with associated calculi. Obstruction was also correctly predicted preoperatively in 7 out of 8 cases in the previous series in which stenosis was demonstrated surgically, so that altogether the cholangiographic diagnosis of partial obstruction was correct in 32 out of 35 cases. On the other hand in 6 cases in the two series combined the cholangiographic diagnosis of obstruction was not confirmed at operation. [It is not stated how often obstruction was diagnosed in patients not subjected to surgery—presumably the error rate in them might well be higher.] In 6 cases in which obstruction was predicted, a carcinoma was found.

The shape of the duct on cholangiography is also stated to help in the diagnosis of partial obstruction. Even with minor degrees it loses its tapered shape and becomes more tubular, while in severe obstruction the biliary radicles are blunted in the same way as the calyces of the kidney in hydronephrosis. However, cholangiography is less useful than pyelography, as hepatic damage and frequent jaundice preclude any possibility of visualization in the vast majority of cases of stricture of the common duct. Cholangiography is recommended as a routine procedure before cholecystectomy, both because it may help in the preoperative diagnosis of stones in the duct, and also to provide a record for comparison if symptoms should recur after operation. *Denys Jennings*

RADIOTHERAPY

1055. Radiation Therapy in the Treatment of Retinoblastoma

I. G. Williams. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 786–795, May, 1957. 9 figs., 7 refs.

The author describes the progress in the treatment of retinoblastoma and the results obtained in 56 cases treated at St. Bartholomew's Hospital, London, since 1929. The radiation treatment described is that to the primary tumour in the eye, aiming at cure with the preservation of some vision. Enucleation is performed only when one-third or more of the retina is involved and the other eye is either normal or the site of a much smaller tumour.

The cases fall into 3 groups. (1) Five cases treated by Foster Moore in the period 1929–34 by radon seed either inserted into the tumour or tied to the sclera over the tumour; of these patients, 4 are alive, 2 having sufficient vision to be able to lead reasonably normal lives. (2) In 1934–48 Stallard treated 15 cases, using radon seeds set in a Stent strip which was sutured to the sclera over the tumour; of these 15 patients, 14 are alive, 9 having sufficient sight to receive normal education. (3) Since 1948 a new type of applicator has been employed, the design of which has finally been refined to consist of a disk of stainless steel containing radioactive cobalt as the radiation source. The applicator is placed in position by attachment to a special clip previously sutured to the sclera in such a position that the applicator lies over the tumour. This technique has been used in a total of 36 cases. In 28 patients (29 eyes) it was used alone, when less than one-third of the retina was involved. At the time of reporting 27 patients (28 eyes) are cured, and 6 patients (7 eyes) have survived for 5 years. In the other 8 cases more than half the retina was involved, and treatment consisted in *x*-ray therapy to a dose of 2,500 r, followed by application of the radioactive cobalt disk to the residue. Only one of

these patients has some vision, 3 are blind, and 4 had to have the eye excised.

Complications of treatment consisted in exudate, haemorrhage, detachment of the retina, and cataract of the lens. The retinal changes occurred particularly in cases in which a large amount of retina was involved by the tumour when treatment was begun. It is pointed out that success with these techniques depends almost entirely on the size of the tumour at the time of treatment. *D. Pearson*

1056. **A Clinical Study of Radiation Cataracts and the Relationship to Dose**

G. R. MERRIAM and E. F. FOCHT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **77**, 759–785, May, 1957. 9 figs., 37 refs.

In an investigation carried out over the past 10 years at the Memorial Center and the Institute of Ophthalmology, Columbia–Presbyterian Medical Center, New York, the records of 100 cases of radiation cataract and of 73 cases in which irradiation was given to the head but in which there were no lens opacities have been studied. All the patients were examined by an ophthalmologist. In an attempt to determine the amount of radiation actually given a skull phantom was devised on which the radiation factors were reduplicated, the dose to the lens being measured by means of a small Baldwin–Farmer condenser ionization chamber placed in a plastic eye in the position of the lens. In cases in which only radium treatment had been given check calculations were also made, assuming a dose rate of 8·4 r per mg. per hour at 1 cm. and applying the law of the inverse square.

The cases were assessed in three groups according to length of treatment, as follows: (1) those given single treatments, all with radium; (2) those given multiple, divided treatments for periods of 3 weeks to 3 months; and (3) those given divided treatments over a period greater than 3 months. In the patients with cataract the dose to the lens had varied from 200 to 6,900 r. (1) Of the 37 patients given a single treatment with radium, 20 developed cataract; the lowest dose at which this occurred was 200 r, no case of cataract being recorded in those receiving less than 175 r. (2) Of those treated for 3 weeks to 3 months, 49 out of 87 had cataract. The lowest dose among these 49 was 400 r, but in some cases receiving up to 1,000 r cataract did not occur. (3) Of the 43 patients treated for over 3 months, 28 had cataract; among these the lowest dose was 550 r, and cataract did not occur in some cases receiving up to 1,100 r. It was therefore concluded that the lowest dose at which cataract always developed was 200 r in the single treatment group and 1,150 r in the two groups given the longer treatments. The time at which the cataract appeared after treatment ranged from 4 months to 28 years 6 months, the interval before onset being shorter with higher doses; or for a given dose the latent period being greater with more protracted treatment. Assessment of the cataracts as stationary or progressive showed that the dose at which all cataracts became progressive was as follows: Group 1 (single treatments) 700 r; Group 2 (3 weeks to 3 months) 1,450 r; and Group 3 (over 3 months) 2,150 r.

The inclusion of a number of cases of retinoblastoma in this study enabled the authors to observe the relative sensitivity of young lenses. The results showed that the incidence of cataract among children under one year of age was 73%, this figure falling to 50% in the age group 1 to 5. In addition, the delay in onset was shorter in the younger age group, and the authors conclude from this that the infant lens is more susceptible to damage by irradiation. *D. Pearson*

1057. **The Association of Tumors and Roentgen-ray Treatment of the Thorax in Infancy**

C. L. SIMPSON and L. H. HEMPELMANN. *Cancer* [*Cancer (Philad.)*] **10**, 42–56, Jan.–Feb., 1957. 3 figs., 44 refs.

It has been the practice for many years in the U.S.A. to irradiate enlarged thymus glands in infancy; it was considered that such infants would provide a useful group for the study of the late effects of radiation. The authors therefore obtained the names of 1,722 children so treated between 1926 and 1951, of whom 1,502 (87%) were eventually traced; the findings in these children were compared with those in 1,933 untreated siblings in order to determine the possible association between early radiotherapy and the later development of tumour or of leukaemia. For study purposes the subjects were divided into six groups roughly according to symptoms, reasons for selection, and plan of treatment; as some were treated before the adoption of the roentgen as a unit, the dose in r was estimated from the known radiation factors. The expected incidence of tumour in the general population of similar age was obtained from the files of the Cancer Registry of New York State. The authors did not see every child, but information was obtained by means of a questionary sent to the parents and the family doctor. All but 31 of the children studied were under one year of age at the time of treatment.

The follow-up showed that 68 treated children and 59 siblings had died. (In some of the siblings death was due to neonatal diseases, a cause which was automatically excluded from the treated group by the method of selection.) Among the treated patients there were 34 cases of malignant tumour, an incidence significantly greater than the expected number, and also greater than the incidence among the siblings. Cancer of the thyroid gland formed the largest group of neoplastic diseases, while the incidence of leukaemia was also significantly increased. The data also suggested an increased number of cases of osteochondroma in the bones falling within the irradiated field. While there was some relationship between the dose of irradiation and the incidence of tumour, it was noted that tumour developed in some cases receiving smaller doses than those previously considered carcinogenic. In conclusion it is suggested that children should not be exposed to irradiation, however small the amount, without very carefully weighing the probable benefits against the possible dangers.

I. G. Williams

1058. **Carcinoma of the Lung**
J. J. NICKSON, E. E. CLIFFTON, and H. SELBY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **77**, 826–835, May, 1957. 8 figs.

The authors analyse 200 cases of pathologically proved carcinoma of the lung in respect of histology, stage, and type of tumour, dosage of radiotherapy, and survival after treatment. The cases, which were selected at random from among those treated at the Memorial Center for Cancer and Allied Diseases, New York, between 1949 and 1952, were classified in four groups: (I) operable and resectable, (II) operable and probably resectable, (III) operable but probably not resectable, and (IV) not operable and not resectable. Criteria for this classification are described in detail and a plea is made for the general adoption of some such grouping in order to facilitate comparison of results.

Surgical resection was the primary treatment for cases in Group I and these are not here reviewed. Cases in Groups II, III, and IV were treated radiotherapeutically with or without previous surgical exploration. Radiotherapy was given either with a 1-MeV machine (H.V.L. 3·4 mm. Pb) or a 250-kV machine (H.V.L. 2 mm. Cu) using a grid technique; the choice of therapy was not random. Dosage (mid-plane values) in cases treated with the 1-MeV machine ranged from 1,000 r in 5 days to 6,200 r in 50 days, the field sizes ranging from 10×12 to 30×16 cm. (parallel opposing pairs). With the 250-kV machine (grid technique) doses (maximal mid-plane) ranged from 1,000 r in 8 days to 6,600 r in 39 days, field sizes ranging from 10×8 to 15×15 cm.

The average period of survival was as follows: Group II, 7·4 months; Group III, 7·6 months; and Group IV, 5·4 months. In those cases in which the patients survived over 12 months the dosage was 2,800 r or more [presumably given over 3 weeks]. The two types of radiotherapy are contrasted, and although superficially a longer survival was obtained after treatment with the 1-MeV apparatus, the fact that the choice of treatment was not random precludes any conclusions being drawn. In certain cases additional treatment with radon seeds was given at the time of thoracotomy, while others received chemotherapeutic agents of the nitrogen mustard and T.E.M. groups. There were no significant findings in either of these groups. *J. G. Stewart*

1059. **Radiation Management of Apical Lung Tumors**
L. L. HAAS, R. A. HARVEY, and C. F. MELCHOR. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 496–525, April, 1957. 12 figs., 23 refs.

The authors review their findings in 18 cases of tumour in the apex of the lung which were treated by irradiation at the University of Illinois College of Medicine, Chicago. In all cases the tumour would appear to have originated in the lung, rather than in the pleura or chest wall. The authors no longer use the term " Pancoast tumour " but recognize the " Pancoast syndrome " when the chest wall is involved. Pain in the shoulder, the arm, or the chest was a prominent feature. In 8 cases conventional *x*-ray treatment was given; 7 of these patients died 3 to 9 months (average 6 months) after the first irradiation; only 2 of them obtained satisfactory relief; the remaining patient was alive and well 11 years later. Of 10 patients treated with 22·5-MeV *x* rays, 2 were alive and well 11 and 27 months respectively after the first irradiation; the average survival time of the remainder was 19·6 months. The palliative effect of the 22·5-MeV *x* rays was striking, and when there were no regional or distant metastases life was undoubtedly prolonged. *J. Boland*

1060. **Dose Distribution and Results in Carcinoma of the Cervix. A Comparison of Conventional High Voltage Therapy Including Vaginal Cone Therapy with Supervoltage Therapy**
R. J. GUTTMANN. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **77**, 803–814, May, 1957. 7 figs., 13 refs.

The author compares the results obtained in the treatment of carcinoma of the uterine cervix in 393 unselected patients by three different techniques during the past 14 years at the Memorial Center for Cancer and Allied Diseases and the Francis Delafield Hospital, New York. The three techniques were: (1) 250-kV external irradiation, intravaginal cone therapy, and radium; (2) 2,000-kV external irradiation and radium; and (3) 2,000-kV *x*-ray or radioactive cobalt irradiation exclusively. (Full details are given in the paper.) A comparison is made of the dose distribution, tolerance to therapy, and complications encountered in the respective techniques, but the 5-year survival rates for all three methods cannot yet be compared because techniques (2) and (3) have not had a 5-year follow-up. The over-all 5-year survival rate by the first technique (301 cases) was 56·5%.

It is the author's view that (1) the immediate tolerance to supervoltage therapy is better than that to conventional therapy; (2) that late complications appear to be less frequent (though he agrees that perhaps sufficient time has not yet elapsed to permit definite conclusions on this point), and (3) the possibility of delivering a homogeneous high dosage throughout the pelvis may produce a better survival rate.
M. P. Cole

1061. **Superficial Malignant Lesions of Bladder Treated by Radioactive Colloidal Gold (^{198}Au)**
P. I. TUOVINEN and K. KETTUNEN. *British Medical Journal* [*Brit. med. J.*] **1**, 1090–1092, May 11, 1957. 7 refs.

A report is presented from the Maria Hospital, Helsinki, of experience with radioactive colloidal gold (^{198}Au) in the treatment of superficial malignant lesions of the bladder since 1955. Intracavitary treatment has the advantage over external irradiation of protecting adjacent organs. The use of gamma-ray sources for this purpose is liable to promote cystitis and fibrosis; ^{198}Au is a more suitable material because of (1) a short half-life (2·7 days), obviating the danger of contamination after a few days, (2) its emission of 95% beta radiation with only 5% gamma radiation, and (3) its ready

availability in colloidal form, preventing resorption. The maximum penetration of the beta particles is 3·8 mm., with half-value layer 0·3 mm.; the maximum effect is therefore confined to the epithelium. The technique is simple; fluid is restricted on the day before treatment and forbidden on the day itself. In a typical case 300 mc. of ^{198}Au in 70 ml. of saline is injected with a lead-protected syringe through an ordinary catheter, retained for 4 to 6 hours, then removed and its radioactivity measured for dose calculation. The bladder is washed out with warm saline. With suitable precautions there is no significant hazard to personnel. With this technique the dose at the mucosal surface is 4,000 to 5,000 r. Three cases are described in detail. In one a dose as low as 1,700 r caused disappearance of a papilliferous tumour without recurrence so far; in another two, treatments with 4,600 r and 3,800 r respectively were only temporarily successful.

The treatment is probably palliative only, since the bladder epithelium retains its tendency to form fresh crops of tumours. Most of the authors' patients had had previous treatment on several occasions by transurethral or suprapubic fulguration. Careful selection of cases is essential. Only the really superficial papillary type, benign or malignant, involving mucosa alone without infiltration is suitable. Multiple thick papillomata are unsuitable, but after small seedlings have been eradicated by means of ^{198}Au small residual growths can be fulgurated. Alternatively, bulky tumours can be removed first, leaving small villous growths to be dealt with by application of ^{198}Au.

There was no radiation sickness in the authors' series. The only reaction was transient epithelitis, as seen cystoscopically for a few weeks. *J. Walter*

1062. **Interstitial Therapy with Radioactive Isotopes.** (Interstitielle Therapie mit radioaktiven Isotopen)
K. E. Scheer. *Strahlentherapie* [*Strahlentherapie*] **102**, 506–510, April, 1957. 4 figs., 3 refs.

Interstitial radium and radon therapy has tended in recent years to be replaced by external irradiation with *x* rays, but radioactive isotopes now provide new sources of radiation with distinct advantages for interstitial use. Radioactive gold (^{198}Au) is particularly useful because of its high specific activity, conveniently short half-life (2·7 days), and the high proportion of beta and low proportion of gamma radiation emitted. Two special uses of ^{198}Au are here described from the Czerny Hospital (University of Heidelberg).

(1) For implantation into the pituitary gland for the treatment of primary tumours or metastatic cancer of the breast 2- to 4-mm. lengths of gold wire 0·8 mm. in diameter are used, being inserted through a needle by the transethmoidal route under radiological control with an image intensifier. General anaesthesia is needed, but the strain on the patient is slight and this form of treatment can be given where surgery would be ruled out. For cancer of the breast 1 or 2 seeds are inserted, while for large tumours 2 or 3 insertions are made in different parts of the gland. A dose of 10 mc. was found at necropsy to have been insufficient, and 20 mc. is now used. No damage to the optic nerves has occurred in over 50 cases, and no radiological damage to the sella. Successful palliation has been achieved in about one-third of the cases treated, the pain often disappearing in such cases within a few days.

(2) Colloidal gold solution can be injected directly into tumours, giving a more uniform distribution than is obtainable by seeds. This method of treatment has been used for growths of the bladder and female genitalia, and for primary and secondary tumours of the lung. Peripheral lung tumours are treated by intercostal injection through several spaces under radiological control, up to 12 punctures being made, while central growths can be injected bronchoscopically through special cannulae. The dosage so far has had to be empirical, masses of 20 to 40 c.cm. receiving 1·5 mc .per c.cm., of 40 to 80 c.cm. 1 mc. per c.cm., and of more than 80 c.cm. 0·7 mc. per c.cm. A total dose of 120 mc. is not exceeded, as a fraction inevitably escapes into the blood stream and may cause leucopenia, anaemia, and thrombocytopenia. *J. Walter*

1063. **New Drugs for Irradiation Sickness**
B. A. Stoll. *Radiology* [*Radiology*] **68**, 380–385, March, 1957. 3 figs., 12 refs.

A controlled trial is described of a series of new drugs for radiation sickness which was carried out at the Peter MacCallum Clinic, Melbourne, Australia, in continuation of an earlier study (Ellis and Stoll, *J. Fac. Radiol.*, 1952, **3**, 207; *Abstracts of World Medicine*, 1952, **12**, 568). The drugs were pyridoxine hydrochloride, chlorpromazine hydrochloride, cyclizine hydrochloride, and "pacatal", a phenothiazine derivative. Lactose tablets were given initially as an inert control and each drug was administered for a week. If symptoms were relieved the drug was continued to the end of the course of treatment, but if there was no relief the drug for the succeeding week was given.

In the previous investigation pyridoxine was found to be the most effective drug, and in the present trial it gave relief of symptoms in almost the same percentage of cases. Pacatal was superior to cyclizine in ambulant patients because of its more rapid elimination and lower toxicity. When each symptom was considered separately, it was seen that vomiting was the easiest symptom to control. Inert tablets give a surprisingly high proportion of relief, vomiting being relieved in 53% to 75% of cases in the present series. The results obtained in 212 cases are set out in tables. No significant statistical superiority of any one drug was observed, but considered to the 10% level of significance pacatal was superior to other drugs in the relief of symptoms of nausea and vomiting, and there was "a suggestion" that both pacatal and chloropromazine were "more efficacious" than the other drugs when irradiation was given below the diaphragm.

In the author's view the symptoms following therapeutic irradiation are identical with those experienced after atomic radiation. Although the cause of radiation sickness is not clear, the symptoms are presumably due to cell destruction. *E. D. Jones*

History of Medicine

1064. **The Development of the Concept of Cerebral Localization in the Nineteenth Century**
A. E. WALKER. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **31**, 99–121, March–April, 1957. 4 figs., bibliography.

By the 18th century the search for the mechanism and seat of the psychic phenomena which comprise the mind had reached the point where it was generally believed that the sense organs were related to a common pool in the brain—the *sensorium commune*—placed variously in the cerebral ventricles, brain stem, corpus callosum, or white matter of the brain. The possibility that psychic functions or the soul could be "spatially localized" was denied by such medical men as Haller and by such philosophers as Kant. During the last 150 years this metaphysical concept of mind has been displaced by the doctrine of cerebral localization.

Paradoxically, it was the pseudo-science of phrenology, despised by the scientific world, which gave the first stimulus to the concept of cerebral localization, for Gall emphasized that the organs of the mind were located independently in the cerebral cortex. Scorn was poured on this thesis, and for 50 years the academic world accepted the findings of Flourens, who, by mechanical stimulation and by ablation, appeared to show that the lower brain stem had a motor function, while intellectual faculties were diffused in an unlocalized fashion in the cerebral hemispheres, which were inexcitable. However, the seed of dissent had been sown, and various observations confirmed that, in fact, stimulation of the cerebral cortex could give rise to movements of the body or extremities. In 1809 Rolando described muscular contractions in a pig after a conductor from a voltaic pile had been introduced into the cerebral hemisphere of the animal.

Localization of function in the cerebral cortex was also being demonstrated, and in 1861 the "foundation stone" of the new theory of cerebral localization was laid down by Broca when he declared that lesions of the left inferior third frontal convolution produced a loss of the faculty of speech but no paralysis of the muscles employed in phonation. The scientific proof for this doctrine was to be furnished by the double means of electrical stimulation and ablation. In 1870 Gustav Fritsch and Eduard Hitzig in Berlin carried out a series of experiments on the cortex of dogs; stimuli to the anterior region were shown to produce motor responses, and muscular contractions occurred in limbs opposite to the side stimulated. The motor centre of the right forelimb was defined by electrical stimulation, and its removal was followed by an obvious disability in that limb.

These findings were not immediately accepted, and as late as 1878 doubts were cast on them by Michael Foster. Further studies, however, confirmed the existence of a cerebral motor centre in animals, while that in man was demonstrated in 1874 by Roberts Bartholow of Cincinnati, who experimented, with consent, on a patient dying from malignant purulent ulcer of the scalp. In the closing years of the 19th century Ferrier, Schäfer, Horsley, Sherrington, and others were occupied in mapping out the excitable areas of the cortex of different animals, and it was not until early in the present century that a serious attempt was made to relate cortical stimulation and the cytoarchitecture of the cerebral cortex. The first detailed approach to this was made by the Vogts, and their work had considerable influence on subsequent research by Foerster, Penfield, Fulton, and Bucy into the structure of the cerebral cortex.

Localization of function in the cortex was also studied by the parallel technique of ablation. Until the late 19th century this aspect of the work was rendered inconclusive by the crude surgical methods available, and the first reliable investigations were conducted by Goltz, who made important observations on decorticated frogs and dogs. As specific functions were demonstrated in differing areas of the cortex, regional excisions were increasingly studied. A full description is given in the present paper of the research that has been carried out on the effects of occipital lobectomy on vision, of frontal ablations on behaviour, and of temporal ablations on both behaviour and hearing. Details are also given of the work that has been done on the function of the motor cortex and the effects of central ablations. The problem which now faces the neurophysiologist is to determine how these functional divisions of the cerebral hemispheres work together to make up the combined whole, which is the mind. *F. M. Sutherland*

1065. **The Discovery of the Pulmonary Circulation: a New Approach**
E. D. COPPOLA. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **31**, 44–77, Jan.–Feb., 1957. 2 figs., bibliography.

The author has attempted to show that the theory of the pulmonary circulation propounded by Ibn an-Nafis in the 13th century was not forgotten, and that, centuries after his death, it may have influenced the direction of the anatomical investigations of Colombo and Valverde, who finally announced to the Western world that the passage of blood through the lungs was a physiological fact.

Colombo, the author of *De re anatomica libri XV* (1559), is best known as one of the "discoverers" of the pulmonary circulation. Six years previously Michael Servetus had published his account of it. The charge of plagiarism on the part of one or the other was contested during the last years of the 19th century, the dispute ending in a stalemate. The present author considers that the important point is not who deserves priority but rather how the discovery was made. In 1556 Juan

Valverde, prosector to Colombo, published a book setting forth the concept of the pulmonary circulation, acknowledging Colombo as his inspiration. However, 300 years earlier an Arab physician of Damascus, Ibn an-Nafis, had described in unequivocal terms the "motion of the blood through the lungs", and it is now known that some of his works were translated by a contemporary of Colombo.

The author's interesting and detailed biography of Realdo Colombo shows that Michelangelo contemplated executing the illustrations for his book on anatomy. Valverde and Colombo not only recognized the impermeability of the septum, but also established, contrary to the teaching of the "infallible" Galen, that the pulmonary vein contained only blood. In these researches Colombo embraced the experimental method, thus anticipating Bacon by 50 years. In addition, Colombo argued that if the vital spirit were engendered within the heart itself, why would the heart require to be nourished with spirituous blood from the coronary artery? Again, the function of all the valves of the heart was a major proof of the pulmonary transit. Another of Colombo's anti-Galenic arguments, based on an erroneous assumption in ignorance of the existence of the bronchial arteries, was that the lung was responsible for making its own spirituous blood, now known as oxygenated blood.

With so much in common between the concepts of Ibn an-Nafis and those of Valverde and Colombo, the author speculates on the possibility that Colombo had learned of Ibn an-Nafis's description. A possible source of this knowledge would be the translations of Andrea Alpago (1547) published in Venice, which might have been transmitted through the person of one Niccolò Massa of Padua (1499–1569). Alternatively, Paolo Alpago, nephew of Andrea, studied medicine at Padua between the years 1527 and 1541, and the possibility is suggested that Ibn an-Nafis's concept of the pulmonary circulation may have been circulating among anatomists there at that time. *Norman F. Smith*

1066. **Procuration of Abortion in Ancient Rome.** (Il procurato aborto nel mondo romano)
L. VILLA. *Pagine di storia della medicina* [*Pagine Storia Med.*] **1**, 24–36, March–April, 1957.

The extent to which voluntary abortion was practised in ancient Rome is not known precisely, but much may be inferred from points discussed by literary writers. Plutarch and Ovid, for instance, both mention an incident (placed at about 396 B.C.) when the matrons of Rome, in order to avenge themselves on their menfolk for passing an anti-feminist law, "agreed among themselves not to remain pregnant, and not to give birth" (Plutarch) and "in order not to bear children blindly thrust the growing foetus from the womb". It is noteworthy that although the practice was considered reprehensible it was not regarded as homicide, and that any tort resulting therefrom was to the rights of the husband, rather than to the State. Cicero's *Pro Cluentio* deals with the case of a husband who was deprived of an heir in this way.

In the general dissolution of morals in Imperial times abortive practices were probably much more widespread. Ovid, Seneca, Suetonius, and Juvenal all mention women resorting to abortion in order to preserve their youth and beauty (except wealthy matrons who "dally with eunuchs and . . . avoid the necessity . . ."). From the end of the 2nd century A.D., however, we find the practice strongly condemned as homicide by the Christian writers, and this view doubtless inspired the Justinian legislation on the subject.

Obstetrics in ancient Rome was the province of the midwife rather than of the doctor (who was only called in when complications arose). It is probable that the midwives were not above acting as abortionists when required. The most complete medical treatise on obstetrics is that of Soranus, who in Chapter 18 of this work describes "The signs of imminent abortion" and discusses the differential diagnosis between spontaneous and induced abortion. In Chapter 19 he discriminates between abortifacients and contraceptives in the light of the Hippocratic injunction "I will not give to any woman an abortifacient drug", and considers it ethical to make use of either method when pregnancy was contra-indicated. He does in fact favour contraception, rating it "better not to conceive than to destroy the embryo", and describes in detail various methods of preventing conception, including "holding back", sneezing, douches, cold drinks, vaginal suppositories, cervical astringents, and physical barriers at the os uteri. Various potions reputed to destroy the embryo are also mentioned, though he considers that their side-effects may be very harmful. Abortive measures included violent exercise, diuretics and emmenagogues, irritative clysters, inunctions of warm olive oil, a warm bath after drinking wine and highly-seasoned foods, and the local application of decoctions and cataplasms. In one passage he gives detailed directions, which comprised *inter alia* the performance of extensive phlebotomy "to relax the parts" and the use of emollient suppositories, followed by a ride in a carriage. He emphasizes the dangers of instrumental intervention, and finally directs that the post-abortum treatment should be "as for an inflammation".

Among other works, the gynaecological writings attributed to Cleopatra include many recipes for love-philtres, potions to promote or prevent conception, and abortifacients—the last comprising a wide variety of substances, mostly of a "magical" nature. Throdorus Priscianus (*circa* 370) has a chapter on abortion in his work *De mulierum passionibus*, which he prefaces with the injunction that it should be resorted to only when the mother is in danger.

In conclusion the present author discusses the divergent interpretations of modern writers on the position of abortion in Roman law. He concludes, however, that laws directed against those who administered love potions and abortifacients were mainly intended to prevent surreptitious poisoning, rather than to uphold the right of the foetus to existence, since the women in whom abortion was thus procured did not fall within their province. On the other hand, voluntary abortion was severely punished as defrauding the husband of his heir

and the State of a citizen; but again, the rights of the unborn child were ignored. Only with the advent of Christian legislation did abortion come to be regarded as equivalent to homicide. *Geoffrey R. Pendrill*

1067. **The Legends of the Poisoning of Mozart.** (Die Legende von Mozarts Vergiftung)
A. GREITHER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **82**, 928–932, June 7, 1957. 1 fig., 22 refs.

Some years after the death of Mozart in 1791 the rumour arose that he had been poisoned; it was even asserted that the composer Salieri had been the human agent and mercury the substance used. The rumour died from lack of evidence, but recently it has been revived by Kerner in several articles in various medical journals. The whole question is here once again fully discussed [perhaps more fully than it deserves] and it is shown that Kerner's articles were inspired by the views of a learned Russian musician—Belsa—who made much of the supposed antagonistic political views of Mozart and Salieri.

The present author gives a detailed account of the symptoms of Mozart's illness, pointing out that they were not those of mercurial poisoning, but were more in keeping with the diagnosis made by the attending physicians; they were in fact similar to those of many other patients in Vienna suffering at that time from a prevalent infectious fever. After full consideration the author concludes as follows. " This new attempt to prove that Mozart died from poisoning is not the result of careful research, but merely a statement apparently designed more to create a sensation than to do service to Mozart or to historical truth ". [A conclusion which, in the abstracter's opinion, is a considerable understatement.] *Zachary Cope*

1068. **Elizabeth Alkin *alias* Parliament Joan**
J. J. KEEVIL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **31**, 17–28, Jan.–Feb., 1957. Bibliography.

Elizabeth Alkin may be regarded as representative of those women who, from a sense of patriotic duty, undertook the nursing of wounded and disabled men during the English Civil War and the widespread fighting of 1642–51. When, during the first Dutch War (1652–3), the State took over certain hospitals, some of these women came forward to staff the hospitals. Elizabeth Alkin's husband was hanged by the Royalists, probably for spying. At the same time she was thanked by the Roundheads for her devotion to the sick and wounded held by the Royalists. The present author infers that she was working among the men who had condemned her husband and was herself a spy. In 1647 she petitioned for recognition of her past services and her position as the widow of a good Roundhead, and the Commons subsequently decided to grant her money and a house for life. After the Royalist defeat at Worcester, however, the next payment (1651) was accompanied by a warning that she should expect no more " in this kind ". " Parliament Joan ", as she had been nicknamed, probably by one of those she nursed, was no longer required, and henceforth the sinister spy was replaced by a character so different that it is difficult to reconcile the two. Later records testify to her compassionate and generous nature. Her fortunes waned as the authorities ceased to be interested in her, and she never received the permanent pension voted by a grateful Parliament.

In 1653 she offered her services to the wounded of the first Dutch War and was drafted to Portsmouth, where she worked indefatigably until her transfer to Harwich in anticipation of a naval battle. She found her own nurses and paid them. In addition, she " disbursed money for the relief of the poor Dutch prisoners ". Some 200 years later Florence Nightingale was to appeal for help in almost the identical terms used by Elizabeth Alkin.

After the war Elizabeth was not needed for intelligence work or for work among the sick and wounded. She returned to London with but three shillings in her purse, and had to employ two nurses to attend her. She turned informer again, but did not receive the monies voted; even her bed was sold before she received a little relief. Her last appeal was made in 1655, but the last surviving record of her is undated. It cannot be substantiated that her request for permission to be buried without charge in the cloister garth of Westminster Abbey was granted. *Norman F. Smith*

1069. **The Influence of the Hunters on Medical Education**
E. FINCH. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **20**, 205–248, April, 1957. 23 figs., 47 refs.

In this, the Hunterian Oration for 1957, the author gives a short account of the development of medical education in Britain before the time of the Hunters, then describes the rise to fame of the Great Windmill Street School of anatomy and medicine, and finally demonstrates the unique influence on medical education of the brothers Hunter by enumerating the names and distinctions gained by their most illustrious pupils. The list is imposing. In London, Edward Jenner, John Abernethy, Astley Cooper, Matthew Baillie, Everard Home, and William Blizard; in Scotland, James Russell and John Thomson; in Ireland, George and James Cleghorn spread the teaching of the Hunters. In the provinces Charles White of Manchester, Edward Alanson of Liverpool, and William Hey of Leeds derived inspiration from the same source. In Philadelphia, Thomas Cadwalader, William Shippen, John Morgan, and Philip Syng Physick founded their methods of teaching on what they had learnt from John Hunter, and similarly in New York, Samuel Bard and Wright Post, both pupils of John Hunter, helped to found what is now the Columbia University. Few men have had greater influence on medical education than the brothers Hunter.

The oration ends with an appreciation of the Nuffield College of Surgical Sciences and a prophecy that it will have a great and beneficial effect on the future of post-graduate surgical education. *Zachary Cope*

1070. **Samuel Plumbe, 1795 to 1837**
R. M. B. MACKENNA. *British Journal of Dermatology* [*Brit. J. Derm.*] **69**, 215–222, June, 1957. 1 fig., 9 refs.